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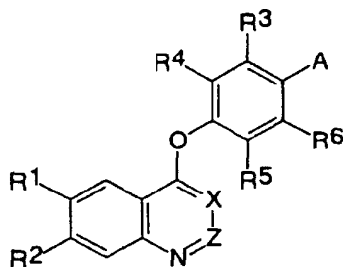
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(57) There are provided compounds which can be used in the treatment of diseases mediated by the autophosphorylation of a PDGF receptor, specifically, compounds which can inhibit neointima formation hypertrophy. The compounds are those represented by formula (I) or pharmacologically acceptable salts or solvates thereof:

wherein R¹ and R² represent hydrogen, alkyl or the like; R³, R⁴, R⁵, and R⁶ represent hydrogen, halogen, alkyl, alkoxy or the like; R¹¹ and R¹² represent hydrogen, alkyl, alkylcarbonyl or the like; and A represents any one of formulae (i) to (x), provided that compounds wherein R³, R⁴, R⁵ and R⁶ represent hydrogen and A represents group (v) wherein u is 0 (zero) and R¹⁹ represents phenyl optionally substituted by halogen, alkyl, or alkoxy are excluded.



(I)

Description**BACKGROUND OF THE INVENTION**Field of the Invention

[0001] The present invention relates to quinoline derivatives and quinazoline derivatives and more particularly to quinoline derivatives and quinazoline derivatives that can be used in the treatment of diseases associated with the autophosphorylation of a PDGF receptor and particularly can inhibit angiostenosis.

Background Art

[0002] PTCA (percutaneous transluminal coronary angioplasty) is widely adopted as therapy useful for ischemic heart diseases resulting from coronary stenosis. Vascular restenosis, which is observed in a frequency of about 30% within 3 to 6 months after the operation of PTCA, however, has become a serious problem associated with long-term prognosis and medical economy. The restenosis is considered attributable to the fact that vascular smooth muscular cells or fibroblasts of the vascular outer membrane are activated, for example, by platelet activation caused by the tear of vascular tunica intima or media, extension stimulation, and vascular endothelial cell injury at the time of catheter therapy and consequently migrate and proliferate and excessively accumulate at injured vascular sites.

[0003] Various growth factors have hitherto been assumed as the vascular smooth muscle cells or fibroblasts activation factors. In particular, since R. Ross et al. have proposed a hypothesis of a injury reaction (N. Engl. J. Med., 295, 369 (1976)), PDGF (platelet-derived growth factor) has drawn attention as one of factors causative of arteriosclerosis and has been also considered as a major factor causative of restenosis from both fundamental and clinical aspects (G.A.A. Ferns et al., Science, 253, 1129 (1991), M.G. Sirois et al., Circulation, 95, 669 (1997), and M. Ueda et al., Am. J. Pathol., 149, 831 (1996) etc.).

[0004] PDGF-R (PDGF receptor) autophosphorylation inhibitory compounds (WO 97/17329 and The FASEB Journal, Vol. 11, pp. 1119 - 1126 (1997)) have been reported up to now.

[0005] For PDGF receptor autophosphorylation inhibitory compounds which have been reported, however, the selectivity for VEGF receptors (such as KDR) and c-kit (SCF receptors) belonging to the PDGF receptor family has not been discussed.

[0006] VEGF is one of major growth factors of vascular endothelial cells (EC), and VEGF receptor inhibitory compounds possibly inhibit the regeneration of EC in injured blood vessels to promote the formation of thrombus and to accelerate angiostenosis.

[0007] Further, SCF is a growth factor involved in the upstream of hematopoietic system and the movement of intestinal tracts, and substances that inhibit receptors of SCF possibly induce hematopoietic failure and intestinal tract movement failure.

[0008] For these reasons, compounds that can selectively inhibit PDGF receptors for c-kit, KDR, and the like are family are expected as anti-restenosis agents that have no significant side effect.

[0009] Although various restenosis inhibitors have been developed up to now, any pharmaceutical compound having potent angiostenosis inhibitory activity has not yet been developed.

SUMMARY OF THE INVENTION

[0010] The present inventors have now found out compounds having PDGF receptor autophosphorylation inhibitory activity.

[0011] The present inventors have also found out compounds inhibiting angiostenosis in rat carotid balloon injury models and porcine coronary balloon injury models.

[0012] The present inventors have further found out compounds having potent PDGF receptor autophosphorylation inhibitory activity and having low VEGF receptor autophosphorylation inhibitory activity.

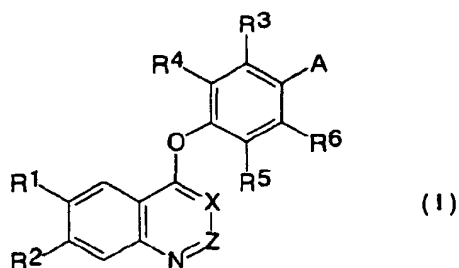
[0013] The present inventors have further found out compounds having PDGF receptor autophosphorylation inhibitory activity and having low c-kit autophosphorylation inhibitory activity.

[0014] An object of the present invention is to provide compounds that can be used in the treatment of diseases mediated by the autophosphorylation of PDGF receptors, particularly compounds having inhibitory activity against angiostenosis.

[0015] Another object of the present invention is to provide compounds that can be used in the treatment of diseases mediated by the autophosphorylation of PDGF receptors and have a low level of side effects attributable to c-kit autophosphorylation inhibitory activity.

[0016] According to the present invention, there is provided a compound represented by formula (I) or a pharmaco-

logically acceptable salt or solvate thereof:



wherein

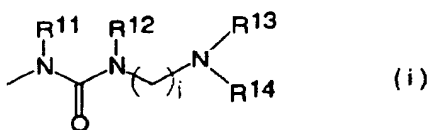
X and Z, which may be the same or different, represent CH or N;

R¹ and R², which may be the same or different, represent a hydrogen atom or C₁₋₄ alkoxy optionally substituted by a halogen atom;

R³, R⁴, R⁵, and R⁶, which may be the same or different, represent a hydrogen atom; a halogen atom; C₁₋₄ alkyl optionally substituted by a halogen atom; C₁₋₄ alkoxy optionally substituted by a halogen atom; nitro; amino; or morphyl;

A represents a group selected from the group consisting of formulae (i) to (x), wherein R¹¹ and R¹², which may be the same or different, represent a hydrogen atom, C₁₋₄ alkyl optionally substituted by a halogen atom, or C₁₋₄ alkylcarbonyl optionally substituted by a halogen atom;

provided that compounds wherein R³, R⁴, R⁵ and R⁶ represent a hydrogen atom and A represents group (v) wherein u is 0 (zero) and R¹⁹ represents phenyl optionally substituted by a halogen atom, C₁₋₄ alkyl, or C₁₋₄ alkoxy are excluded:

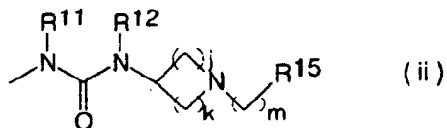


wherein

i is an integer of 0 to 10,

R¹³ and R¹⁴, which may be the same or different, represent a hydrogen atom; C₁₋₆ alkyl optionally substituted by a halogen atom; or phenyl optionally substituted by a halogen atom or C₁₋₄ alkyl optionally substituted by a halogen atom,

R¹³ and R¹⁴ may form a five- to seven-membered saturated or unsaturated heterocyclic ring optionally containing one or more additional hetero-atoms together with the nitrogen atom to which they are attached, and this heterocyclic ring is optionally substituted by a halogen atom or C₁₋₄ alkyl optionally substituted by a halogen atom, or, R¹³ or R¹⁴ may form C₁₋₄ alkylene optionally substituted by a halogen atom together with R¹²;



wherein

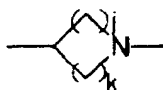
j is an integer of 0 to 3,

k is an integer of 0 to 3, provided that

both j and k are not 0 (zero),

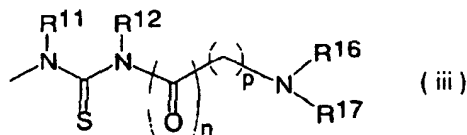
m is an integer of 0 to 2,

carbon atoms in the following



are optionally substituted by one or more C_{1-4} alkyl groups, which may be the same or different, optionally substituted by a halogen atom, and

R^{15} represents a hydrogen atom; cyclic C_{3-7} alkyl optionally substituted by a halogen atom; phenyl optionally substituted by C_{1-6} alkyl or a halogen atom; or C_{1-4} alkoxy carbonyl;



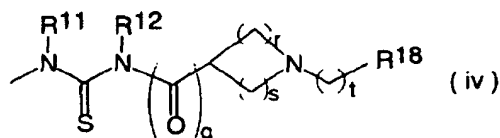
wherein

n is 0 (zero) or 1,

p is an integer of 0 to 10, and

R^{16} and R^{17} , which may be the same or different, represent a hydrogen atom; C_{1-6} alkyl optionally substituted by a halogen atom; C_{1-4} alkyl carbonyl optionally substituted by a halogen atom; cyclic C_{3-7} alkyl optionally substituted by C_{1-4} alkyl optionally substituted by a halogen atom; or phenyl optionally substituted by a halogen atom or C_{1-4} alkyl optionally substituted by a halogen atom, or

R^{16} and R^{17} may form a five- to seven-membered saturated or unsaturated heterocyclic ring optionally containing one or more additional hetero-atoms together with the nitrogen atom to which they are attached, this heterocyclic ring is optionally condensed with another one or two carbocyclic or heterocyclic ring to form a ten- to twelve-membered saturated or unsaturated bicyclic carbocyclic ring or heterocyclic ring or a ten- to fifteen-membered saturated or unsaturated tricyclic carbocyclic ring or heterocyclic ring, and these heterocyclic rings are optionally substituted by an oxygen atom or C_{1-4} alkyl optionally substituted by a halogen atom;



wherein

q is 0 (zero) or 1,

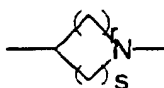
r is an integer of 0 to 3,

s is an integer of 0 to 3, provided that

both r and s are not 0 (zero),

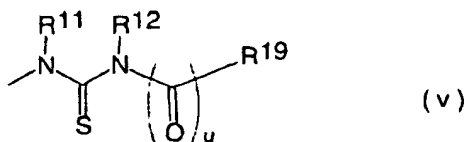
t is an integer of 0 to 2,

carbon atoms in the following



are optionally substituted by one or more C_{1-4} alkyl groups, which may be the same or different, and

R^{18} represents a hydrogen atom; phenyl optionally substituted by a halogen atom or C_{1-6} alkyl optionally substituted by a halogen atom; or C_{1-4} alkoxy carbonyl optionally substituted by a halogen atom;



wherein

10 u is 0 (zero) or 1,
R¹⁹ represents

15 (1) phenyl which is optionally substituted by C₁₋₁₀ alkyl optionally substituted by a halogen atom; C₁₋₁₀ alkoxy optionally substituted by a halogen atom; -NR³¹R³² wherein R³¹ and R³², which may be the same or different, represent a hydrogen atom or C₁₋₄ alkyl optionally substituted by a halogen atom; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(2) phenoxy of which the phenyl portion is optionally substituted by C₁₋₁₀ alkyl optionally substituted by a halogen atom; C₁₋₁₀ alkoxy optionally substituted by a halogen atom; -NR³¹R³² wherein R³¹ and R³² are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

20 (3) cyclic C₃₋₇ alkyl which is optionally condensed with another carbocyclic ring or heterocyclic ring to form an eight- to twelve-membered bicyclic saturated or unsaturated carbocyclic ring or heterocyclic ring and the carbocyclic ring and the heterocyclic ring are optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom; phenyl optionally substituted by a halogen atom; cyclic C₃₋₇ alkyl optionally substituted by a halogen atom; or a halogen atom,

25 (4) a five- to seven-membered saturated or unsaturated heterocyclic ring which is optionally condensed with another carbocyclic or heterocyclic ring to form a ten- to twelve-membered bicyclic saturated or unsaturated heterocyclic ring optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom, or a halogen atom,

(5) C₁₋₁₆ alkyl,

(6) C₂₋₆ alkenyl, or

30 (7) C₂₋₆ alkynyl,

wherein (5) C₁₋₁₆ alkyl, (6) C₂₋₆ alkenyl, and (7) C₂₋₆ alkynyl are optionally substituted by one or more of the following groups:

35 (a) phenyl optionally substituted by C₁₋₁₀ alkyl optionally substituted by a halogen atom; C₁₋₁₀ alkoxy optionally substituted by a halogen atom; -NR³¹R³² wherein R³¹ and R³² are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(b) phenoxy of which the phenyl portion is optionally substituted by C₁₋₁₀ alkyl optionally substituted by a halogen atom; C₁₋₁₀ alkoxy optionally substituted by a halogen atom; -NR³¹R³² wherein R³¹ and R³² are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

40 (c) phenylthio of which the phenyl portion is optionally substituted by C₁₋₁₀ alkyl optionally substituted by a halogen atom; C₁₋₁₀ alkoxy optionally substituted by a halogen atom; -NR³¹R³² wherein R³¹ and R³² are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(d) -NR³³R³⁴ wherein R³³ and R³⁴ are as defined in R¹³ and R¹⁴,

45 (e) cyclic C₃₋₇ alkyl which is optionally condensed with another carbocyclic ring or heterocyclic ring to form an eight- to twelve-membered bicyclic saturated or unsaturated carbocyclic ring or heterocyclic ring and the carbocyclic ring and the heterocyclic ring are optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom; phenyl optionally substituted by a halogen atom; or a halogen atom,

50 (f) a five- to seven-membered saturated or unsaturated heterocyclic ring which is optionally condensed with another carbocyclic ring or heterocyclic ring to form a ten- to twelve-membered bicyclic saturated or unsaturated heterocyclic ring optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom, or a halogen atom,

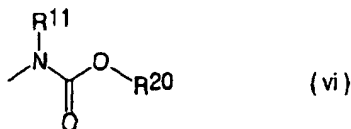
(g) naphthyl,

(h) cyano,

(i) C₁₋₄ alkylthio optionally substituted by a halogen atom,

55 (j) a halogen atom, or

(k) alkoxycarbonyl optionally substituted by a halogen atom;



wherein

R²⁰ represents

(1) phenyl optionally substituted by C₁₋₆ alkyl optionally substituted by a halogen atom; C₁₋₆ alkoxy optionally substituted by a halogen atom; -NR³⁵R³⁶ wherein R³⁵ and R³⁶, which may be the same or different, represent a hydrogen atom or C₁₋₄ alkyl optionally substituted by a halogen atom; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(2) cyclic C₃₋₇ alkyl which is optionally condensed with another carbocyclic ring or heterocyclic ring to form an eight- to twelve-membered bicyclic saturated or unsaturated carbocyclic ring or heterocyclic ring and the carbocyclic ring and the heterocyclic ring are optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom, or a halogen atom,

(3) a five- to seven-membered saturated or unsaturated heterocyclic ring which is optionally condensed with another carbocyclic ring or heterocyclic ring to form a ten- to twelve-membered bicyclic saturated or unsaturated heterocyclic ring optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom, or a halogen atom,

(4) C₁₋₂₀ alkyl,

(5) C₂₋₆ alkenyl, or

(6) C₂₋₆ alkynyl, and

wherein (4) C₁₋₂₀ alkyl, (5) C₂₋₆ alkenyl, and (6) C₂₋₆ alkynyl are optionally substituted by one or more of the following groups:

(a) phenyl optionally substituted by C₁₋₆ alkyl optionally substituted by a halogen atom; C₁₋₆ alkoxy optionally substituted by a halogen atom; -NR³⁵R³⁶ wherein R³⁵ and R³⁶ are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(b) phenoxy of which the phenyl portion is optionally substituted by C₁₋₆ alkyl optionally substituted by a halogen atom; C₁₋₆ alkoxy optionally substituted by a halogen atom; -NR³⁵R³⁶ wherein R³⁵ and R³⁶ are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(c) phenylthio of which the phenyl portion is optionally substituted by C₁₋₆ alkyl optionally substituted by a halogen atom; C₁₋₆ alkoxy optionally substituted by a halogen atom; -NR³⁵R³⁶ wherein R³⁵ and R³⁶ are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

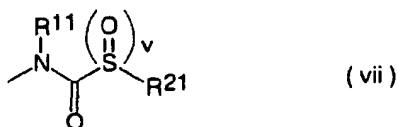
(d) -NR³⁷R³⁸ wherein R³⁷ and R³⁸ are as defined in R¹³ and R¹⁴,

(e) cyclic C₃₋₇ alkyl which is optionally condensed with another carbocyclic ring or heterocyclic ring to form an eight- to twelve-membered bicyclic saturated or unsaturated carbocyclic ring or heterocyclic ring and the carbocyclic ring and the heterocyclic ring are optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom, or a halogen atom,

(f) a five- to seven-membered saturated or unsaturated heterocyclic ring which is optionally condensed with another carbocyclic ring or heterocyclic ring to form a ten- to twelve-membered bicyclic saturated or unsaturated heterocyclic ring optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom, or a halogen atom,

(g) naphthyl, or

(h) cyano;



wherein

v is an integer of 0 to 2,

R²¹ represents

(1) phenyl optionally substituted by C₁₋₆ alkyl optionally substituted by a halogen atom; C₁₋₆ alkoxy optionally substituted by a halogen atom; -NR³⁹R⁴⁰ wherein R³⁹ and R⁴⁰, which may be the same or different, represent a hydrogen atom or C₁₋₄ alkyl optionally substituted by a halogen atom; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(2) cyclic C₃₋₇ alkyl which is optionally condensed with another carbocyclic ring or heterocyclic ring to form an eight- to twelve-membered bicyclic saturated or unsaturated carbocyclic ring or heterocyclic ring and the carbocyclic ring and the heterocyclic ring are optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom, or a halogen atom,

(3) a five- to seven-membered saturated or unsaturated heterocyclic ring which is optionally condensed with another carbocyclic ring or heterocyclic ring to form a ten- to twelve-membered bicyclic saturated or unsaturated heterocyclic ring optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom, or a halogen atom,

(4) C₁₋₂₀ alkyl,

(5) C₂₋₆ alkenyl, or

(6) C₂₋₆ alkynyl, and

wherein (4) C₁₋₂₀ alkyl, (5) C₂₋₆ alkenyl, and (6) C₂₋₆ alkynyl are optionally substituted by one or more of the following groups:

(a) phenyl optionally substituted by C₁₋₆ alkyl optionally substituted by a halogen atom; C₁₋₆ alkoxy optionally substituted by a halogen atom; -NR³⁹R⁴⁰ wherein R³⁹ and R⁴⁰ are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(b) phenoxy of which the phenyl portion is optionally substituted by C₁₋₆ alkyl optionally substituted by a halogen atom; C₁₋₆ alkoxy optionally substituted by a halogen atom; -NR³⁹R⁴⁰ wherein R³⁹ and R⁴⁰ are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(c) phenylthio of which the phenyl portion is optionally substituted by C₁₋₆ alkyl optionally substituted by a halogen atom; C₁₋₆ alkoxy optionally substituted by a halogen atom; -NR³⁹R⁴⁰ wherein R³⁹ and R⁴⁰ are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(d) -NR⁴¹R⁴² wherein R⁴¹ and R⁴² are as defined in R¹³ and R¹⁴,

(e) cyclic C₃₋₇ alkyl which is optionally condensed with another carbocyclic ring or heterocyclic ring to form an eight- to twelve-membered bicyclic saturated or unsaturated carbocyclic ring or heterocyclic ring and the carbocyclic ring and the heterocyclic ring are optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom, or a halogen atom,

(f) a five- to seven-membered saturated or unsaturated heterocyclic ring which is optionally condensed with another carbocyclic ring or heterocyclic ring to form a ten- to twelve-membered bicyclic saturated or unsaturated heterocyclic ring optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom, or a halogen atom,

(g) naphthyl, or

(h) cyano;



wherein

w is an integer of 1 to 4,

L represents -O-, -S(=O)y-, wherein y is an integer of 0 to 2, or -N(-R¹¹)-,

M represents -O-, -C(=O)-O-, -S(=O)z-, wherein z is an integer of 0 to 2, -N(-R¹²)-, -C(=O)-N(-R¹²)-, or -C(=O)-,

R²² represents a hydrogen atom; C₁₋₄ alkyl optionally substituted by a halogen atom; or phenyl optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom, C₁₋₄ alkoxy optionally substituted by a halogen atom, nitro, amino, or a halogen atom,

when M represents -N(-R¹²)- or -C(=O)-N(-R¹²)-, R²² and R¹² may form a five- to seven-membered saturated or unsaturated heterocyclic ring optionally containing one or more additional hetero-atoms together with the nitrogen atom to which they are attached, this heterocyclic ring is optionally condensed with another carbocyclic ring or heterocyclic ring to form a ten- to twelve-membered bicyclic saturated or unsaturated heterocyclic ring, and these heterocyclic rings are optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom; phenyl; benzyl; or piperidine;



wherein R^{23} represents a hydrogen atom or C_{1-4} alkyl optionally substituted by a halogen atom; and



wherein R^{24} and R^{25} , which may be the same or different, represent a hydrogen atom or C_{1-4} alkyl optionally substituted by a halogen atom.

[0017] The compounds according to the present invention are useful for the treatment of diseases mediated by the autophosphorylation of PDGF receptors.

DETAILED DESCRIPTION OF THE INVENTION

Compound

[0018] The terms "alkyl," "alkoxy," "alkenyl," and "alkynyl" as used herein as a group or a part of a group respectively mean straight chain or branched chain alkyl, alkoxy, alkenyl, and alkynyl.

[0019] C_{1-6} alkyl is preferably C_{1-4} alkyl.

[0020] C_{1-10} alkyl is preferably C_{1-8} alkyl.

[0021] C_{1-16} alkyl is preferably C_{1-13} alkyl.

[0022] C_{1-20} alkyl is preferably C_{1-18} alkyl.

[0023] C_{1-6} alkoxy is preferably C_{1-4} alkoxy.

[0024] C_{1-10} alkoxy is preferably C_{1-8} alkoxy.

[0025] C_{2-6} alkenyl is preferably C_{2-4} alkenyl.

[0026] C_{2-6} alkynyl is preferably C_{2-4} alkynyl.

[0027] Examples of C_{1-6} alkyl include methyl, ethyl, n-propyl, isopropyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, and n-hexyl.

[0028] Examples of C_{1-6} alkoxy include methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, i-butoxy, s-butoxy, and t-butoxy.

[0029] Examples of C_{2-6} alkenyl include allyl, butenyl, pentenyl, and hexenyl.

[0030] Examples of C_{2-6} alkynyl include 2-propynyl, butynyl, pentynyl, and hexynyl.

[0031] The expression "alkyl optionally substituted by" as used herein means alkyl, of which one or more hydrogen atoms are substituted by one or more substituents which may be the same or different, or unsubstituted alkyl. It will be understood by a person skilled in the art that the maximum number of the substituents can be determined depending upon the number of substitutable hydrogen atoms on the alkyl group. This will apply to groups having substituents other than alkyl.

[0032] The term "halogen atom" as used herein means a fluorine, chlorine, bromine, or iodine atom.

[0033] The saturated or unsaturated five- to seven-membered heterocyclic ring contains one or more hetero-atoms selected from oxygen, nitrogen, and sulfur atoms. Examples of the saturated or unsaturated five- to seven-membered heterocyclic group include pyridyl, piperidino, piperazino, morpholino, imidazolyl, triazolyl, tetrazolyl, oxazolyl, thiazolyl, pyrrolidinyl, and pyrazolyl.

[0034] The five- to seven-membered saturated or unsaturated heterocyclic group may be condensed with another saturated or unsaturated carbocyclic ring or heterocyclic ring to form a ten- to twelve-membered bicyclic ring or a ten- to fifteen-membered tricyclic ring. Condensed bicyclic groups include indanyl, quinolyl, and quinazolinyl. Condensed tricyclic groups include phenythiazyl, phenoxazyl, and dihydrodibenzoazepinyl.

[0035] Cyclic C_{3-7} alkyl may be condensed with another saturated or unsaturated carbocyclic ring or heterocyclic ring to form an eight- to twelve-membered bicyclic saturated or unsaturated carbocyclic ring or heterocyclic ring. Condensed bicyclic groups include indanyl, quinolyl, and quinazolinyl.

[0036] In group (i), i is preferably an integer of 0 to 4, more preferably 1 to 3.

[0037] An example of preferred group (i) is a group wherein i is an integer of 1 to 3, R^{13} and R^{14} , which may be the same or different, represent C_{1-4} alkyl or may form a five- to seven-membered saturated heterocyclic ring optionally substituted by C_{1-4} alkyl together with the nitrogen atom, to which they are attached.

[0038] In group (ii), j is preferably an integer of 1 or 2. k is preferably an integer of 1 or 2. m is preferably an integer of 1 or 2.

[0039] An example of preferred group (ii) is a group wherein j is 1 or 2, k is 1 or 2, m is 1 or 2, and R^{15} represents

optionally substituted phenyl.

[0040] In group (iii), p is preferably an integer of 0 to 3.

[0041] An example of preferred group (iii) is a group wherein n is 0 (zero), p is an integer of 1 to 3, and R¹⁶ and R¹⁷, which may be the same or different, represent C₁₋₄ alkyl or may form a five- to seven-membered saturated heterocyclic ring optionally substituted by C₁₋₄ alkyl or an oxygen atom together with the nitrogen atom, to which they are attached.

[0042] Another example of preferred group (iii) is a group wherein n is 1 and p is 0 (zero).

[0043] In group (iv), r is preferably an integer of 1 or 2. s is preferably an integer of 1 or 2. t is preferably an integer of 0 or 1.

[0044] An example of preferred group (iv) is a group wherein q is 0 (zero), r is 1 or 2, s is 1 or 2, t is 1 or 2, and R¹⁸ represents optionally substituted phenyl.

[0045] In group (v), the phenyl and phenoxy groups presented by R¹⁹ are optionally substituted by C₆₋₁₀ alkyl or C₆₋₁₀ alkoxy, preferably C₆₋₈ alkyl or C₆₋₈ alkoxy.

[0046] In group (v), the alkyl, alkenyl, and alkynyl groups presented by R¹⁹ are optionally substituted by phenyl, phenoxy, or phenylthio, and this phenyl, phenoxy, or phenylthio group is optionally substituted by C₆₋₁₀ alkyl or C₆₋₁₀ alkoxy, preferably C₆₋₈ alkyl or C₆₋₈ alkoxy.

[0047] An example of preferred group (v) is a group wherein u is 1 and R¹⁹ represents C₁₋₄ alkyl substituted by optionally substituted phenyl.

[0048] An example of preferred group (vi) is a group wherein R²⁰ represents optionally substituted phenyl or C₁₋₆ alkyl optionally substituted by optionally substituted phenyl.

[0049] In group (viii), w is preferably an integer of 1 to 3.

[0050] When L represents -O-, preferably, M represents -O-, -C(=O)-O-, -N(-R¹²)-, -C(=O)-N(-R¹²)-, or -C(=O)-. When L represents -S(=O)y-, preferably, M represents -O-. When L represents -N(-R¹¹)-, preferably, M represents -O-.

[0051] An example of preferred group (viii) is a group wherein w is an integer of 1 to 3, L represents -O-, M represents -O- or -C(=O)-O-, and R²² represents optionally substituted phenyl.

[0052] Examples of preferred compounds represented by formula (I) according to the present invention include the following compounds:

compounds wherein X represents CH or N and Z represents CH;

compounds wherein R¹ and R² represent C₁₋₄ alkoxy and at least one of R³, R⁴, R⁵ and R⁶ represents a group other than a hydrogen atom;

compounds wherein R¹ and R² represent C₁₋₄ alkoxy, R³ represents a group other than a hydrogen atom, and R⁴, R⁵, and R⁶ represent a hydrogen atom;

compounds wherein R¹ and R² represent C₁₋₄ alkoxy, A represents group (i), wherein i is an integer of 1 to 3, and R¹³ and R¹⁴, which may be the same or different, represent C₁₋₄ alkyl or may form a five- to seven-membered saturated heterocyclic ring optionally substituted by C₁₋₄ alkyl together with the nitrogen atom, to which they are attached and, more preferably, X represents CH or N and Z represents CH;

compounds wherein R¹ and R² represent C₁₋₄ alkoxy, R³, R⁴, R⁵ and R⁶ represent a hydrogen atom, A represents group (i), wherein i is an integer of 1 to 3, and R¹³ and R¹⁴, which may be the same or different, represent C₁₋₄ alkyl or may form a five- to seven-membered saturated heterocyclic ring optionally substituted by C₁₋₄ alkyl together with the nitrogen atom to which they are attached and, more preferably, X represents CH or N and Z represents CH;

compounds wherein R¹ and R² represent C₁₋₄ alkoxy, R³ represents a group other than a hydrogen atom, R⁴, R⁵ and R⁶ represent a hydrogen atom, A represents group (i) wherein i is an integer of 1 to 3, and R¹³ and R¹⁴, which may be the same or different, represent C₁₋₄ alkyl or may form a five- to seven-membered saturated heterocyclic ring optionally substituted by C₁₋₄ alkyl together with the nitrogen atom, to which they are attached, and, more preferably, X represents CH or N and Z represents CH;

compounds wherein R¹ and R² represent C₁₋₄ alkoxy, R³ represents nitro, R⁴, R⁵, and R⁶ represent a hydrogen atom, A represents group (i) wherein i is an integer of 1 to 3, and R¹³ and R¹⁴, which may be the same or different, represent C₁₋₄ alkyl or may form a five- to seven-membered saturated heterocyclic ring optionally substituted by C₁₋₄ alkyl together with the nitrogen atom, to which they are attached, and, more preferably, X represents CH or N and Z represents CH;

compounds wherein X represents N, Z represents CH, R¹ and R² represent C₁₋₄ alkoxy, R³ represents nitro, R⁴, R⁵, and R⁶ represent a hydrogen atom, A represents group (i) wherein i is 2, and R¹³ and R¹⁴, which may be the same or different, represent C₂₋₃ alkyl or may form a six-membered saturated heterocyclic ring optionally substituted by C₁₋₄ alkyl together with the nitrogen atom, to which they are attached;

compounds wherein R¹ and R² represent C₁₋₄ alkoxy, A represents group (ii) wherein j is 1 or 2, k is 1 or 2, m is 1 or 2, and R¹⁵ represents optionally substituted phenyl and, more preferably, X represents CH or N and Z represents CH;

compounds wherein R¹ and R² represent C₁₋₄ alkoxy, R³, R⁴, R⁵, and R⁶ represent a hydrogen atom, A represents

group (ii) wherein j is 1 or 2, k is 1 or 2, m is 1 or 2, and R¹⁵ represents optionally substituted phenyl;
 compounds wherein R¹ and R² represent C₁₋₄ alkoxy, R³ represents a group other than a hydrogen atom, R⁴, R⁵,
 and R⁶ represent a hydrogen atom, A represents group (ii) wherein j is 1 or 2, k is 1 or 2, m is 1 or 2, and R¹⁵
 represents optionally substituted phenyl and, more preferably, X represents CH or N and Z represents CH;
 5 compounds wherein R¹ and R² represent C₁₋₄ alkoxy, A represents group (iii) wherein n is 0 (zero), p is an integer
 of 1 to 3, and R¹⁶ and R¹⁷, which may be the same or different, represent C₁₋₄ alkyl or may form a five- to seven-
 membered saturated heterocyclic ring optionally substituted by C₁₋₄ alkyl or an oxygen atom together with the
 nitrogen atom, to which they are attached, and, more preferably, X represents CH or N and Z represents CH;
 10 compounds wherein R¹ and R² represent C₁₋₄ alkoxy, R³, R⁴, R⁵, and R⁶ represent a hydrogen atom, A represents
 group (iii) wherein n is 0 (zero), p is an integer of 1 to 3, and R¹⁶ and R¹⁷, which may be the same or different,
 represent C₁₋₄ alkyl or may form a five- to seven-membered saturated heterocyclic ring optionally substituted by
 C₁₋₄ alkyl or an oxygen atom together with the nitrogen atom, to which they are attached, and, more preferably, X
 represents CH or N and Z represents CH;
 15 compounds wherein R¹ and R² represent C₁₋₄ alkoxy, R³ represents a group other than a hydrogen atom, R⁴, R⁵,
 and R⁶ represent a hydrogen atom, A represents group (iii) wherein n is 0 (zero), p is an integer of 1 to 3, and R¹⁶
 and R¹⁷, which may be the same or different, represent C₁₋₄ alkyl or may form a five- to seven-membered saturated
 heterocyclic ring optionally substituted by C₁₋₄ alkyl or an oxygen atom together with the nitrogen atom, to which
 they are attached, and, more preferably, X represents CH or N and Z represents CH;
 20 compounds wherein R¹ and R² represent C₁₋₄ alkoxy, A represents group (iv) wherein q is 0 (zero), r is 1 or 2, s
 is 1 or 2, t is 1 or 2, and R¹⁸ represents optionally substituted phenyl, and, more preferably, X represents CH or N
 and Z represents CH;
 compounds wherein R¹ and R² represent C₁₋₄ alkoxy, R³, R⁴, R⁵ and R⁶ represent a hydrogen atom, and A rep-
 resents group (iv) wherein q is 0 (zero), r is 1 or 2, s is 1 or 2, t is 1 or 2, and R¹⁸ represents optionally substituted
 phenyl;
 25 compounds wherein R¹ and R² represent C₁₋₄ alkoxy, R³ represents a group other than a hydrogen atom, R⁴, R⁵,
 and R⁶ represent a hydrogen atom, and A represents group (iv) wherein q is 0 (zero), r is 1 or 2, s is 1 or 2, t is 1
 or 2, and R¹⁸ represents optionally substituted phenyl, and, more preferably, X represents CH or N and Z represents
 CH;
 compounds wherein R¹ and R² represent C₁₋₄ alkoxy and A represents group (v), wherein u is 1, and R¹⁹ represents
 30 optionally substituted phenyl, or C₁₋₄ alkyl substituted by optionally substituted phenyl, and, more preferably, X
 represents CH or N and Z represents CH;
 compounds wherein R¹ and R² represent C₁₋₄ alkoxy, R³, R⁴, R⁵, and R⁶ represent a hydrogen atom, A represents
 group (v) wherein u is 1, R¹⁹ represents optionally substituted phenyl, or C₁₋₄ alkyl substituted by optionally sub-
 stituted phenyl;
 35 compounds wherein R¹ and R² represent C₁₋₄ alkoxy, R⁵ represents a group other than a hydrogen atom, R³, R⁴,
 and R⁶ represent a hydrogen atom, and A represents group (v) wherein u is 1, R¹⁹ represents optionally substituted
 phenyl, or C₁₋₄ alkyl substituted by optionally substituted phenyl, and, more preferably, X represents CH or N and
 Z represents CH;
 compounds wherein R¹ and R² represent C₁₋₄ alkoxy and A represents group (vi) wherein R²⁰ represents optionally
 40 substituted phenyl or C₁₋₆ alkyl optionally substituted by optionally substituted phenyl, and, more preferably, X
 represents CH or N and Z represents CH;
 compounds wherein R¹ and R² represent C₁₋₄ alkoxy and A represents group (vii) wherein R²¹ represents optionally
 substituted phenyl, or C₁₋₆ alkyl optionally substituted by optionally substituted phenyl, and, more preferably, X
 represents CH or N and Z represents CH;
 45 compounds wherein R¹ and R² represent C₁₋₄ alkoxy and A represents group (viii) wherein w is an integer of 1 to
 3, L represents -O-, M represents -O- or -C(=O)-O-, R²² represents optionally substituted phenyl, and, more pref-
 erably, X represents CH or N and Z represents CH;
 compounds wherein R¹ and R² represent C₁₋₄ alkoxy and A represents group (viii) wherein, when L represents
 -O-, M represents -O-, -C(=O)-O-, -N(-R¹²)-, -C(=O)-N(-R¹²)-, or -C(=O)-; when L represents -S(=O)y-, M repre-
 50 sents -O-; and when L represents -N(-R¹¹)-, M represents -O-, and, more preferably, X represents CH or N and Z
 represents CH;
 compounds wherein R¹ and R² represent C₁₋₄ alkoxy and A represents group (iii), wherein n is 1 and p is 0 (zero),
 and, more preferably, X represents CH or N and Z represents CH; and
 55 compounds wherein R¹ and R² represent C₁₋₄ alkoxy, R³ represents morpholyl, R⁴, R⁵, and R⁶ represent a hydro-
 gen atom, and A represents group (x), and, more preferably, X represents CH or N and Z represents CH.

[0053] Examples of particularly preferred compounds according to the present invention include compounds de-
 scribed in Examples 1 to 1209.

[0054] In addition to the compounds described in Examples 1 to 1209, the following compounds may be included in examples of particularly preferred compounds according to the present invention:

N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}-N-(4-piperidinobutyl)urea;
 N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}-N-(3-piperidinopropyl)urea;
 N-[4-(diethylamino)butyl]-N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}urea;
 N-[3-(diethylamino)propyl]-N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}urea;
 N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N-(4-methylpiperazino)urea; and
 N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N-(4-methylpiperazino)urea.

[0055] Examples of more preferred compounds according to the present invention are the following compounds:

N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}-N'-(2-piperidinoethyl)urea; and
 N-[2-(diethylamino)ethyl]-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}urea.

[0056] One or more enantiomeric carbon atoms, which form enantiomer configuration, may exist in the compounds represented by formula (I). The compounds represented by formula (I) include all enantiomers.

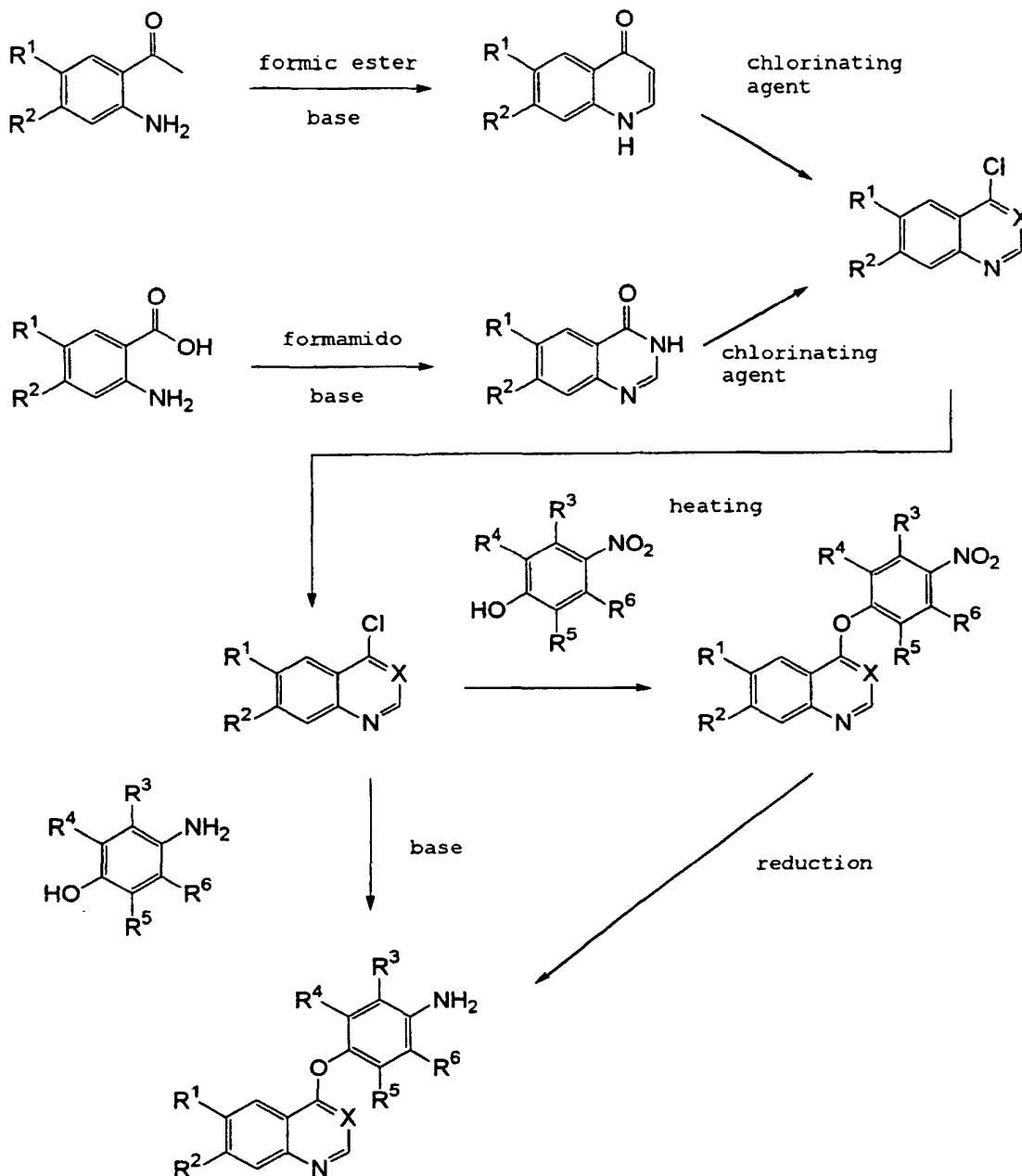
[0057] Pharmacologically acceptable salts of the compounds represented by formula (I) include acid addition salts. Acid addition salts include: salts with inorganic acids such as hydrochloric acid, sulfuric acid, phosphoric acid, hydrobromic acid, and nitric acid; or organic acids such as maleic acid, fumaric acid, malic acid, oxalic acid, tartaric acid, succinic acid, citric acid, acetic acid, lactic acid, methanesulfonic acid, and p-toluenesulfonic acid.

[0058] Pharmacologically acceptable solvates of the compounds represented by formula (I) include hydrates and ethanolates.

Production process of compounds

[0059] (1) Compounds represented by formula (I), wherein A represents groups (i), (ii), (xi), and (x), may be produced, for example, according to scheme 1 and scheme 2.

Scheme 1



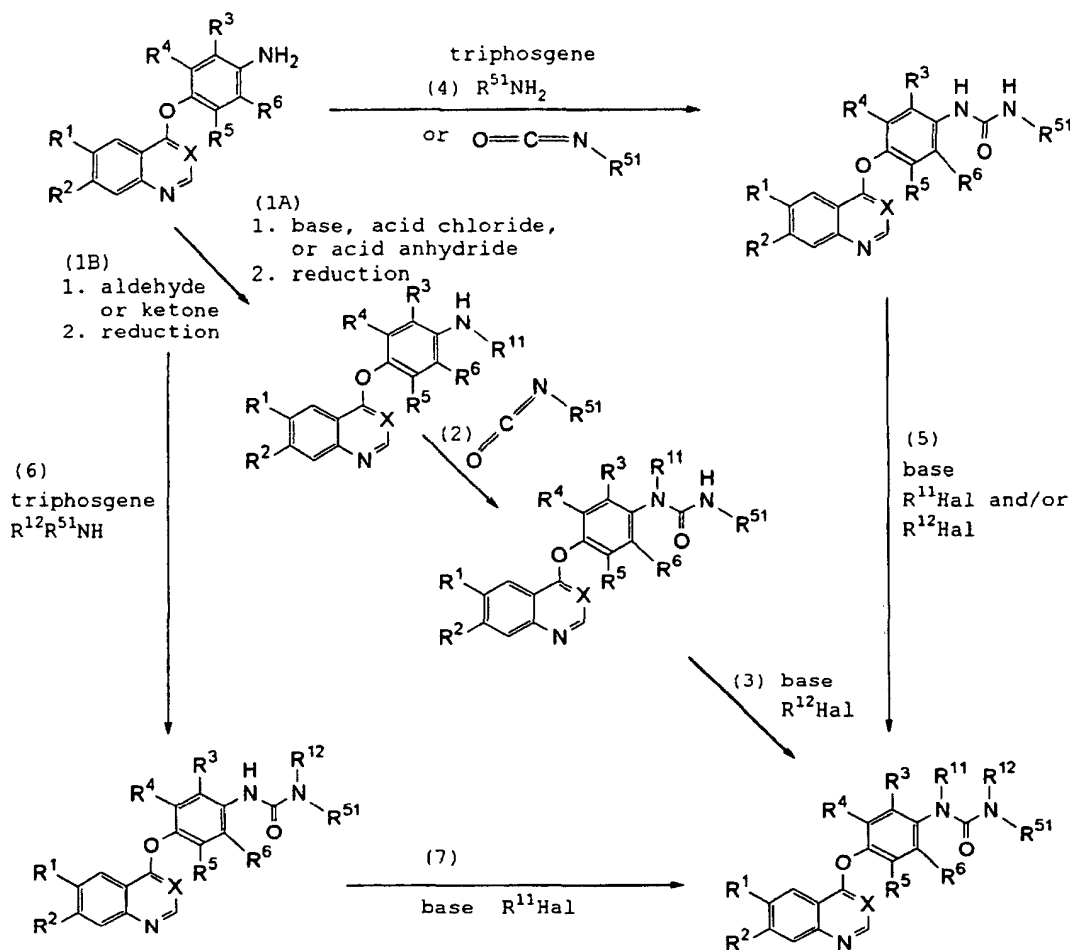
[0060] Starting compounds necessary for the synthesis of the compounds according to the present invention are commercially available or can be easily produced by a conventional method.

[0061] Quinolone derivatives as an intermediate may be synthesized according to the method described, for example, in WO 97/17329. Further, 4-chloroquinoline derivatives may be synthesized by a conventional method described, for example, in Org. Synth. Col., Vol. 3, 272 (1955), Acta Chim. Hung., 112, 241 (1983) or WO 98/47873. Further, 4-chloroquinazoline derivatives may be synthesized by a conventional method described, for example, in J. Am. Chem. Soc., 68, 1299 (1946), J. Am. Chem. Soc., 68, 1305 (1946) or Dai-Yukikagaku, supervised by Kotake, Vol. 17, p. 150, Asakura Publishing Co., Ltd., 1967.

[0062] 4-(Nitrophenoxy)quinoline derivatives or corresponding quinazoline derivatives may be synthesized by react-

ing nitrophenol with a 4-chloroquinoline derivative or a corresponding quinazoline derivative in the presence or absence of a suitable solvent. 4-(Aminophenoxy)quinoline derivatives or corresponding quinazoline derivatives may be synthesized by stirring a 4-(nitrophenoxy)quinoline derivative or a corresponding quinazoline derivative in a suitable solvent, for example, N,N-dimethylformamide, in the presence of a catalyst, for example, palladium hydroxide-carbon or palladium-carbon) in a hydrogen atmosphere. Alternatively, 4-(aminophenoxy)quinoline derivatives or corresponding quinazoline derivatives may be synthesized by reacting an aminophenol derivative with a 4-chloroquinoline derivative or a corresponding quinazoline derivative in the presence of a base, for example, sodium hydride.

Scheme 2



[0063] A substituent can be introduced into R¹¹ by reacting a 4-(aminophenoxy)quinoline derivative or a corresponding quinazoline derivative with an acid chloride or an acid anhydride in the presence of a base and then reducing the reaction product with lithium aluminum hydride or the like (step 1A).

[0064] Alternatively, a substituent can be introduced into R¹¹ by reacting a 4-(aminophenoxy)quinoline derivative or a corresponding quinazoline derivative with an aldehyde or a ketone to form an imine compound and then reducing the imine compound with sodium cyanoborohydride or the like (step 1B).

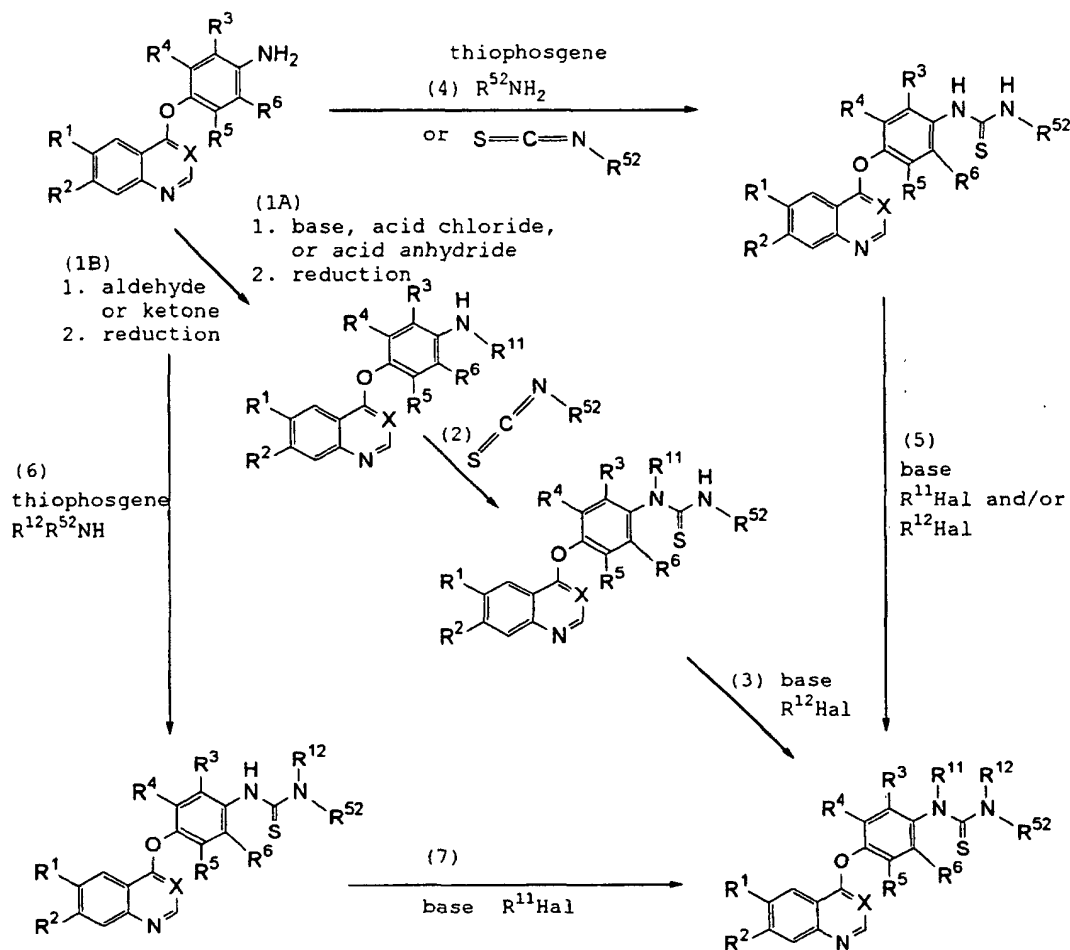
[0065] Compounds represented by formula (I) may be produced by reacting a derivative having a substituent at R¹¹ with an isocyanate derivative (O=C=N-R⁵¹ wherein R⁵¹ represents a portion of groups (i) and (ii) not having a urea portion according to a conventional method (step 2) and, if necessary, reacting the reaction product with a suitable alkylating agent (R¹²Hal) in the presence of a base, for example, sodium hydride (step 3).

[0066] R¹¹ and R¹² may also be introduced by reacting a urea derivative, wherein R¹⁰ and/or R¹¹ represent a hydrogen atom, with a suitable alkylating agent (R¹¹Hal or R¹²Hal) in the presence of a base, for example, sodium hydride (steps 5 and 7).

[0067] Urea derivatives, wherein R^{11} and/or R^{12} represent a hydrogen atom, may be produced by reacting a 4-(aminophenoxy)quinoline derivative or a corresponding quinazoline derivative produced in scheme 1 with an isocyanate derivative according to a conventional method, or by adding triphosgene in the presence of a base, for example, triethylamine and then reacting the mixture with a suitable alkylamine ($R^{51}NH_2$ or $R^{11}R^{51}NH$) (steps 4 and 6).

[0068] (2) Compounds represented by formula (I), wherein A represents groups (iii), (iv), and (v), may be produced, for example, according to scheme 3.

Scheme 3



[0069] A substituent can be introduced into R^{11} by reacting a 4-(aminophenoxy)quinoline derivative or a corresponding quinazoline derivative with an acid chloride or an acid anhydride in the presence of a base and then reducing the reaction product with lithium aluminum hydride or the like (step 1A).

[0070] Alternatively, a substituent can be introduced into R^{11} by reacting a 4-(aminophenoxy)quinoline derivative or a corresponding quinazoline derivative with an aldehyde or a ketone to form an imine derivative and then reducing the imine derivative with sodium cyanoborohydride or the like (step 1B).

[0071] Compounds represented by formula (I) may be produced by reacting a derivative having a substituent at R^{11} with an isothiocyanate derivative, ($S=C=N-R^{52}$ wherein R^{52} represents a portion of groups (iii), (iv), and (v), not having a thiourea portion according to a conventional method (step 2) and, if necessary, reacting the reaction product with a suitable alkylating agent ($R^{12}Hal$) in the presence of a base, for example, sodium hydride (step 3).

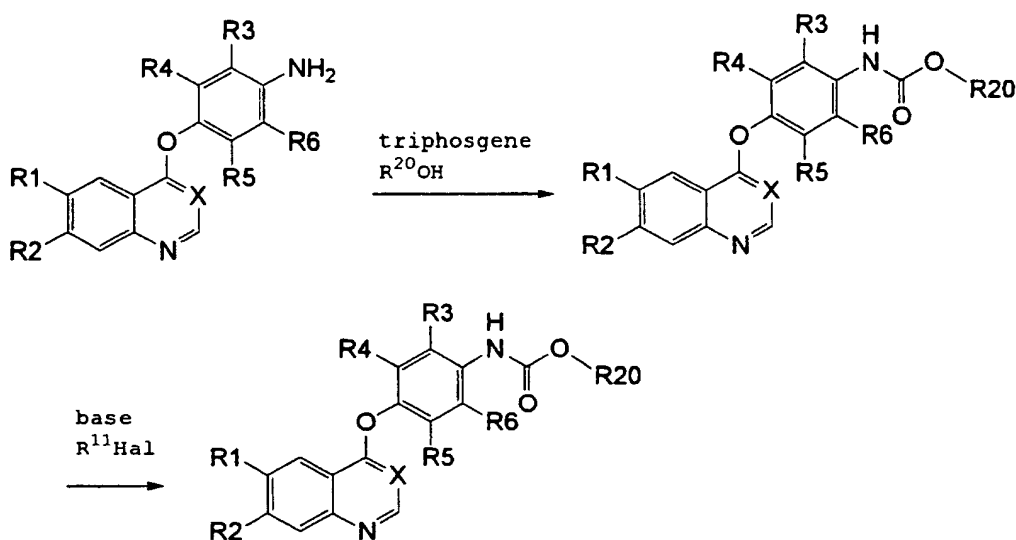
[0072] R^{11} and R^{12} may also be introduced by reacting a thiourea derivative, wherein R^{11} and/or R^{12} represent a hydrogen atom, with a suitable alkylating agent ($R^{11}Hal$ or $R^{12}Hal$) in the presence of a base, for example, sodium hydride (steps 5 and 7).

[0073] Thiourea derivatives, wherein R^{11} and/or R^{12} represent a hydrogen atom, may be produced by reacting a

4-(aminophenoxy)quinoline derivative or a corresponding quinazoline derivative produced in scheme 1 with an isothiocyanate derivative ($S=C=N-R^{52}$) according to a conventional method, or by adding thiophosgene in the presence of a base, for example, triethylamine and then reacting the mixture with a suitable alkylamine ($R^{52}NH_2$ or $R^{11}R^{52}NH$) (steps 4 and 6).

[0074] (3) Compounds represented by formula (I), wherein A represents group (vi), may be produced, for example, according to scheme 4.

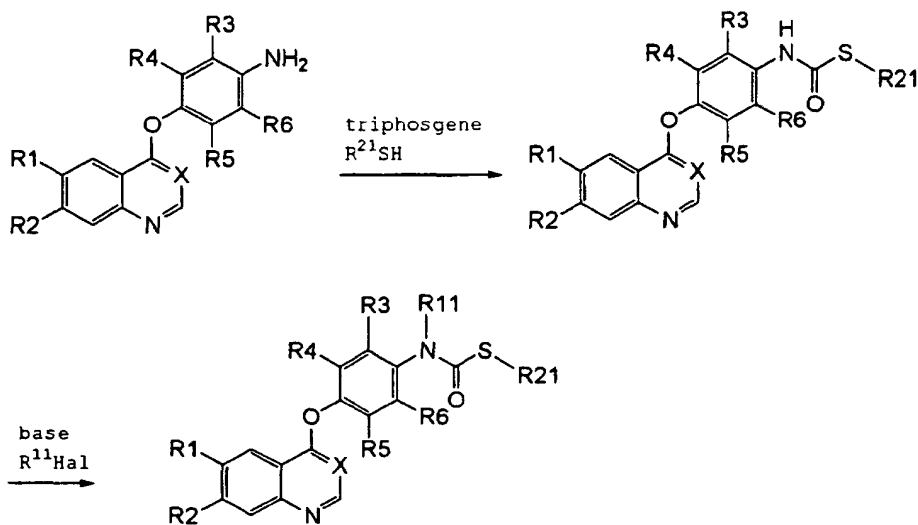
Scheme 4



[0075] Urethane derivatives, wherein R^{11} and/or R^{12} represent a hydrogen atom, may be produced according to a conventional method by adding triphosgene to a 4-(aminophenoxy)quinoline derivative or a corresponding quinazoline derivative produced according to scheme 1 in the presence of a base, for example, triethylamine and then reacting the mixture with a suitable alcohol ($R^{20}OH$). R^{11} may be introduced by reacting a urethane derivative, wherein R^{11} represents a hydrogen atom, with a suitable alkylating agent ($R^{11}Hal$) in the presence of a base, for example, sodium hydride.

[0076] (4) Compounds represented by formula (I), wherein A represents group (vii), may be produced, for example, according to scheme 5.

Scheme 5

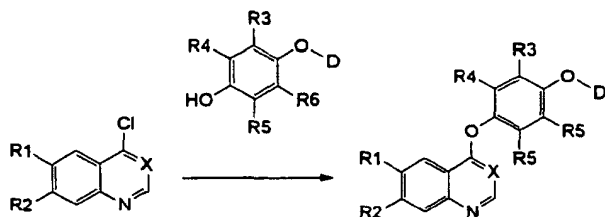


[0077] Thiocarbamate derivatives, wherein R¹¹ and/or R¹² represent a hydrogen atom (v = 0), may be produced by adding triphosgene to a 4-(aminophenoxy)quinoline derivative or a corresponding quinazoline derivative produced in scheme 1 in the presence of a base, for example, triethylamine according to a conventional method and then reacting the mixture with a suitable thiol (R²¹SH). R¹¹ may be introduced by reacting a thiocarbamate derivative, wherein R¹¹ represents a hydrogen atom, with a suitable alkylating agent (R¹¹Hal) in the presence of a base, for example, sodium hydride.

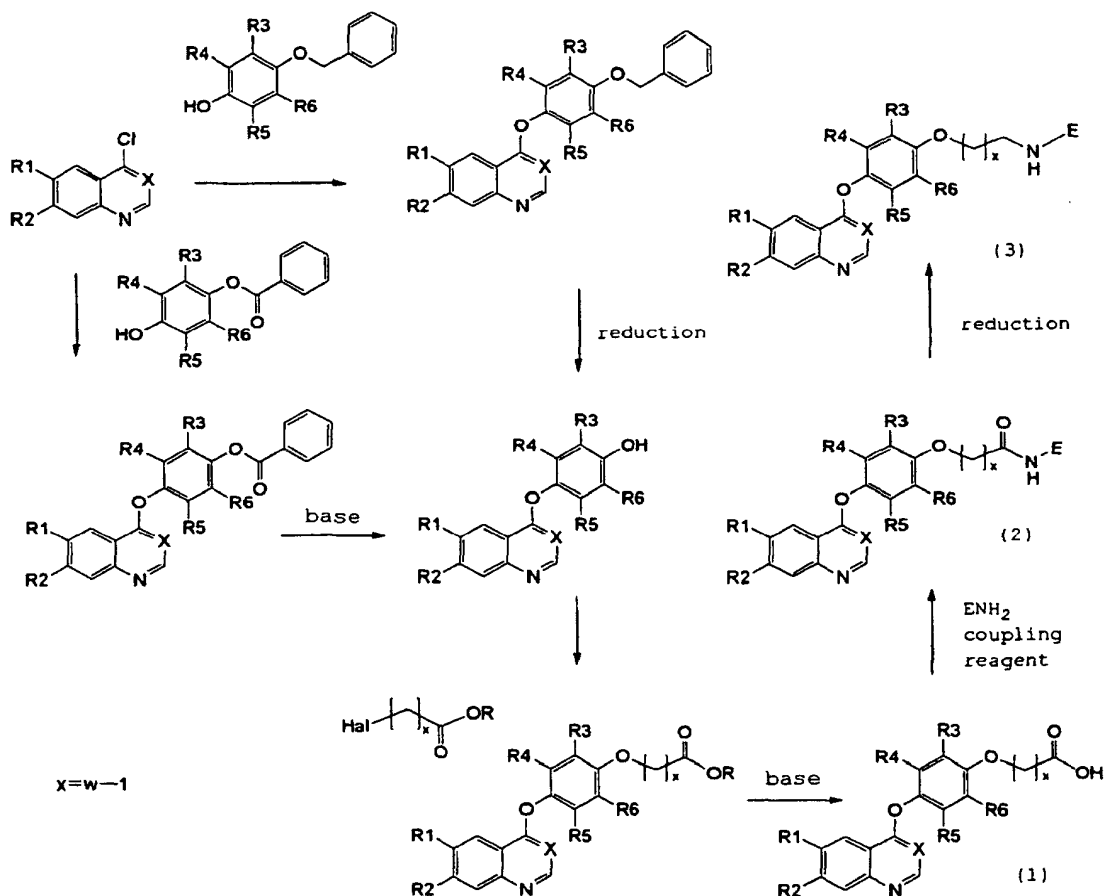
[0078] Oxidation derivatives (v = 1) may be produced by oxidizing the thiocarbamate derivative with an oxidizing agent such as m-chloroperbenzoic acid. Further, oxidation derivatives (v = 2) may be produced by oxidizing a thiocarbamate derivative with an oxidizing agent such as potassium permanganate or oxone.

[0079] (5) Compounds represented by formula (I), wherein A represents groups (viii) and (ix), may be produced, for example, according to schemes 6, 7, and 8.

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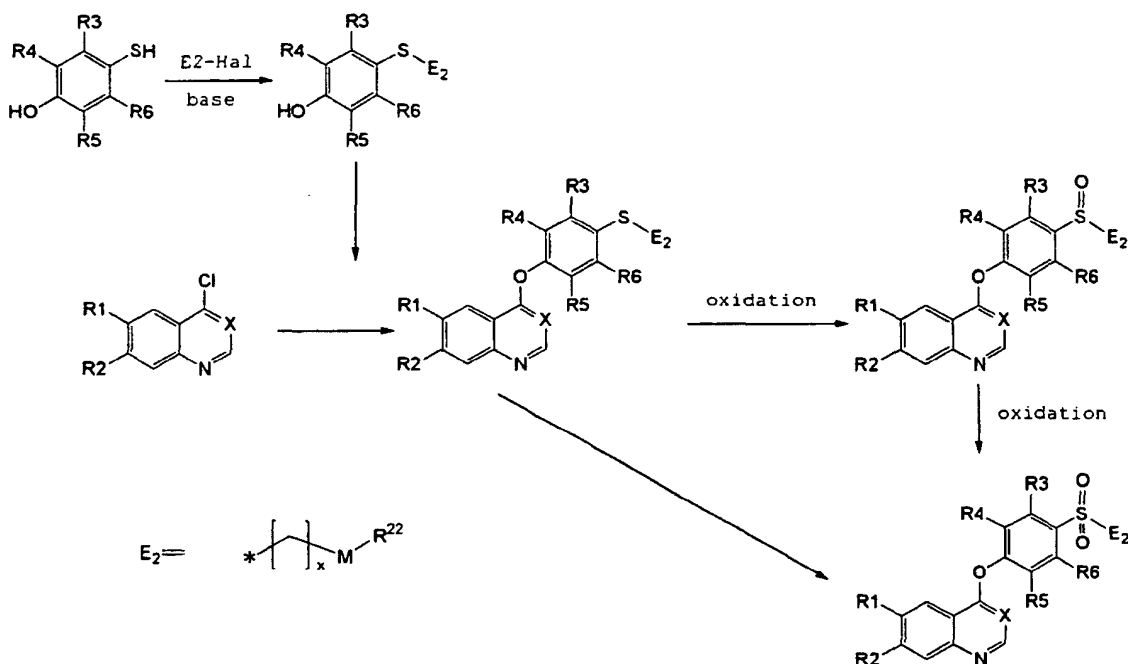
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[0082] 4-(Hydroxyphenoxy)quinoline derivatives or corresponding quinazoline derivatives may be synthesized by deprotecting a 4-(benzyloxyphenoxy)quinoline derivative or a corresponding quinazoline derivative in a suitable solvent, for example, N,N-dimethylformamide, in the presence of a catalyst, for example, palladium hydroxide-carbon or

palladium-carbon in a hydrogen atmosphere. 4-(Hydroxyphenoxy)quinoline derivatives or corresponding quinazoline derivatives may also be synthesized by deprotecting the benzoyl group in the 4-(benzoyloxyphenoxy)quinoline derivative or corresponding quinazoline derivative under basic conditions, for example, using sodium hydroxide.

[0083] Carboxylic acid compound (1) is produced by reacting a 4-(hydroxyphenoxy)quinoline derivative or a corresponding quinazoline derivative with a ω -halogenated alkyl carboxylic acid ester under basic conditions, for example, using sodium hydride and then deprotecting the ester under basic conditions, for example, using sodium hydroxide. Amide derivative (2) may be produced by reacting carboxylic acid compound (1) with an amine in the presence of a coupling reagent, for example, N,N'-dicyclohexylcarbodiimide. Subsequently, reduced derivative (3) may be produced by reducing amide derivative (2) with diborane, lithium aluminum hydride or the like (scheme 6-2).

Where L = S (scheme 7):



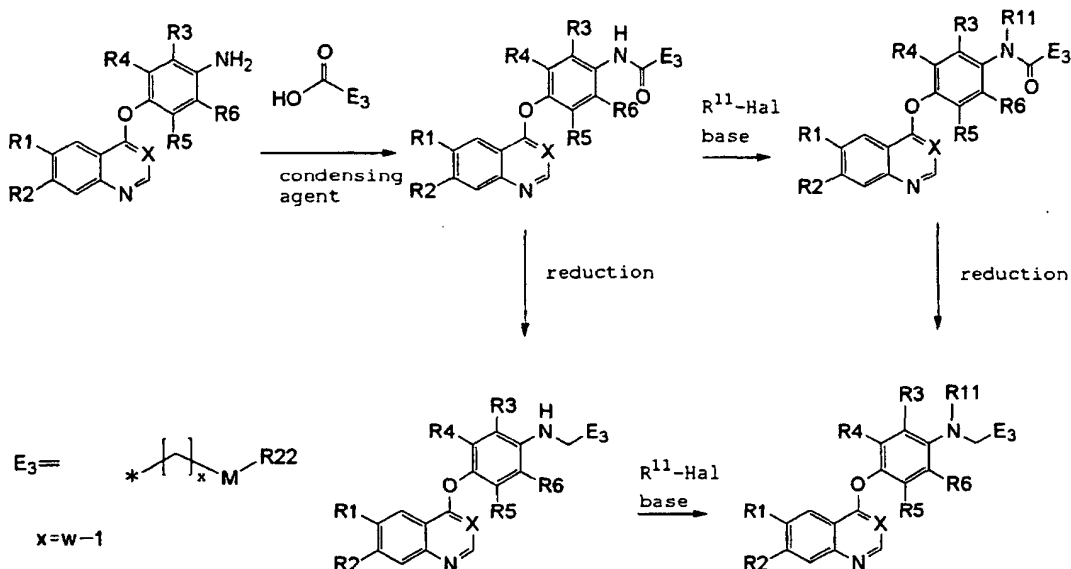
[0084] S-Alkyl-substituted phenols may be produced by reacting a 4-hydroxythiophenol derivative with a suitable alkyl halide derivative in the presence or absence of a suitable solvent under basic conditions, for example, using potassium carbonate. Thio derivatives may be synthesized by reacting the S-alkyl-substituted phenol with a 4-chloroquinoline derivative or a corresponding quinazoline derivative.

[0085] Sulfoxide derivatives may be produced by oxidizing the thio derivative with an oxidizing agent such as m-chloroperbenzoic acid. Sulfone derivatives may be produced by oxidizing the thio derivative with an oxidizing agent such as potassium permanganate or oxone, or by oxidizing the sulfoxide derivative with an oxidizing agent such as potassium permanganate or oxone.

Where $L = NR^{11}$ (scheme 8)

$L = -NR^{11}-$

$M=O$



[0086] A reduced derivative may be produced by reacting a fatty acid with a 4-(aminophenoxy)quinoline derivative or a corresponding quinazoline derivative produced by a conventional method in the presence of a coupling reagent to give an amide derivative and reducing the amide derivative with diborane, lithium aluminum hydride or the like. R^{11} may be introduced by reacting a reduced derivative, wherein R^{11} represents a hydrogen atom, with a suitable alkylating agent ($R^{11}\text{Hal}$) in the presence of a base, for example, sodium hydride. Alternatively, R^{11} may be introduced by reacting an amide derivative, wherein R^{11} represents a hydrogen atom, with a suitable alkylating agent ($R^{11}\text{Hal}$) in the presence of a base, for example, sodium hydride. Further, a reduced derivative having a substituent at R^{11} may be produced by reducing the derivative with diborane, lithium aluminum hydride or the like.

Use of compounds

[0087] The compounds according to the present invention inhibit, in vitro, PDGF-R autophosphorylation and the growth and migration of vascular smooth muscle cells induced by PDGF stimulation (see Pharmacological Test Examples 1 and 2). The autophosphorylation of PDGF receptors mediates diseases, for example, ischemic diseases involving blood vessel occlusion or angiostenosis induced by angiopathy, ischemic diseases involving blood vessel occlusion or angiostenosis induced by vascular autotransplantation or allotransplantation, and diseases involving cell proliferation and organ fibrosis induced by PDGF, for example, chronic rheumatism, PDGF-dependent tumors such as glioma, cirrhosis, pulmonary fibrosis, and occlusion of arteriovenous shunt resulting, for example, from dialysis of patients suffering from renal failure (Gordon A. A. Ferns et al., Science, Vol. 253, pp 1129 - 1132 (1991), Martin G Sirois et al., Circulation, Vol. 95, No. 3, pp 669 - 675 (1997), Marukka Myllarniemi et al., The FASEB Journal, Vol. 11, pp 1119 - 1126 (1997), H. Ohnishi et al., Life Science, Vol. 28, pp 1641 - 1646 (1981), J. Gastroenterol. Vol. 32, pp 496 - 501 (1997), Toxicol. Appl. Pharmacol. Vol. 149, pp 120 - 126 (1998), and Am. J. Pathol. Vol. 148, pp 785 - 800 (1996)). Further, the compounds according to the present invention have low VEGF-R inhibitory activity (Pharmacological Test Example 5). Compounds, which do not inhibit VEGF-R, are expected not to accelerate angiostenosis. Furthermore, the compounds according to the present invention inhibit, in vivo, neointima formation hypertrophy of injured blood vessels (Pharmacological Test Examples 4 and 6). Therefore, the compounds according to the present invention can be used in the treatment of diseases mediated by the autophosphorylation of PDGF receptors, particularly ischemic

diseases involving blood vessel occlusion/angiostenosis induced by blood vessel injury or vascular autotransplantation or allotransplantation.

[0088] The compounds according to the present invention have low c-kit autophosphorylation inhibitory activity. The c-kit autophosphorylation inhibitory activity crucially affects hematopoiesis and intestinal tract movements (Experimental Medicine, Vol. 11, No. 13, pp 42 - 53). Therefore, the present invention can provide compounds which do not cause any significant side effect attributable to c-kit autophosphorylation inhibitory activity.

[0089] Pharmaceutical compositions comprising compounds of the present invention as an active ingredient can be administered to human and non-human animals orally or parenterally by administration routes, for example, intravenous administration, intramuscular administration, subcutaneous administration, rectal administration, or percutaneous administration. Therefore, the pharmaceutical composition comprising the compound according to the present invention as active ingredient may be formulated into suitable dosage forms according to the administration routes.

[0090] Specifically, oral preparations include tablets, capsules, powders, granules, and syrups, and parental preparations include injections, suppositories, tapes, and ointments.

[0091] These various preparations may be prepared by conventional methods, for example, with commonly used component, such as excipients, disintegrants, binders, lubricants, colorants, and diluents.

[0092] Excipients include, for example, lactose, glucose, corn starch, sorbit, and crystalline cellulose; disintegrants include, for example, starch, sodium alginate, gelatin powder, calcium carbonate, calcium citrate, and dextrin; binders include, for example, dimethylcellulose, polyvinyl alcohol, polyvinyl ether, methylcellulose, ethylcellulose, gum arabic, gelatin, hydroxypropylcellulose, polyvinyl pyrrolidone, carboxymethylcellulose sodium salt, and chromophore; lubricants include, for example, talc, magnesium stearate, polyethylene glycol, and hydrogenated vegetable oils.

[0093] In preparing injections, if necessary, for example, buffers, pH adjustors, stabilizers, tonicity agents, and preservatives may be added.

[0094] The dose of the compound according to the present invention in the pharmaceutical composition may vary depending upon the dosage form. In general, however, the dose is about 0.5 to 50% by weight, preferably about 1 to 20% by weight, based on the whole composition.

[0095] The dose may be appropriately determined depending upon, for example, the age, weight, sex, difference in diseases, and severity of condition of patients, and the active ingredient may be administered, for example, in an amount of 0.1 to 100 mg/kg, preferably 0.1 to 30 mg/kg. This dose can be administered at a time daily or divided doses of several times daily.

EXAMPLES

[0096] The present invention will be described in more detail with reference to the following examples, though it is not limited to these examples only.

Production Example 1: 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-nitroaniline

[0097] Sodium hydride (60 wt%, 0.20 g) was added to dimethyl sulfoxide (15 ml), and the mixture was stirred at room temperature for 10 min. 4-Amino-3-nitrophenol (0.77 g) was added thereto, and the mixture was stirred at room temperature for 10 min. Next, 4-chloro-6,7-dimethoxyquinazoline (1.12 g) was added thereto, and the mixture was stirred at 100°C for 3 hr. Water was added to the reaction solution, followed by extraction with chloroform. The chloroform layer was then washed with a 1 N aqueous sodium hydroxide solution and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and methanol was added to the residue to prepare a suspension. The precipitated crystal was collected by suction filtration to give the title compound (1.10 g, yield 64%).

[0098] ¹H-NMR (CDCl₃-d₁, 400 MHz) : δ 4.07 (s, 3H), 4.08 (s, 3H), 6.10 - 6.15 (m, 2H), 6.92 (d, J = 9.0 Hz, 1H), 7.34 (s, 1H), 7.35 (dd, J = 9.0 Hz, J = 2.7 Hz, 1H), 7.52 (s, 1H), 8.06 (d, J = 2.9 Hz, 1H), 8.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 343 (M⁺+1)

Production Example 2: 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline

[0099] 4-Chloro-6,7-dimethoxyquinazoline (10.23 g) and 2-fluoro-4-nitrophenol (14.37 g) were suspended in monochlorobenzene (100 ml), and the suspension was heated under reflux overnight. The solvent was removed by distillation under the reduced pressure, and the residue was washed with toluene, was filtered, and was dried. The crystal thus obtained was then suspended in an aqueous sodium hydroxide solution, and the suspension was filtered, followed by drying to give 4-(3-fluoro-4-nitrophenoxy)-6,7-dimethoxyquinoline (14.2 g, yield 90%). 4-(2-Fluoro-4-nitrophenoxy)-6,7-dimethoxy-quinoline (4.57 g) was dissolved in ethyl acetate/N,N-dimethylformamide/triethylamine (100 ml/100 ml/20 ml) to prepare a solution. Palladium hydroxide (1.2 g) was added to the solution, and the mixture was stirred in a hydrogen atmosphere at room temperature overnight. After filtration through Celite, the solvent was removed by dis-

tillation under the reduced pressure. A saturated aqueous sodium hydrogencarbonate solution was added to the residue, and the mixture was extracted with chloroform. The organic layer was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure to quantitatively give 4.27 g of the title compound.

$^1\text{H-NMR}$ ($\text{CDCl}_3\text{-d}_1$, 400 MHz) : δ 3.85 (m, 2H), 4.07 (s, 3H), 4.08 (s, 3H), 6.50 - 6.60 (m, 3H), 7.02 - 7.07 (m, 1H), 7.55 - 7.65 (m, 2H), 8.48 (d, $J = 5.6$ Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 315 ($M^+ + 1$)

Production Example 3: 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline

[0100] Sodium hydride (60 wt%, 0.72 g) was added to dimethyl sulfoxide (10 ml), and the mixture was stirred at 50°C for 20 min. 4-Amino-3-chlorophenol hydrochloride (1.61 g) was added thereto, and the mixture was stirred at room temperature for 10 min. Next, 4-chloro-6,7-dimethoxyquinoline (1.00 g) was added thereto, and the mixture was stirred at 100°C overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The chloroform layer was then washed with a saturated aqueous sodium hydrogencarbonate solution and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. Methanol was added to the residue, and the precipitated crystal was collected by suction filtration to give the title compound (0.80 g, yield 60%).

$^1\text{H-NMR}$ ($\text{CDCl}_3\text{-d}_1$, 400 MHz): δ 4.06 (s, 3H), 4.07 (s, 3H), 6.36 (d, $J = 5.4$ Hz, 1H), 6.65 (dd, $J = 8.5$ Hz, $J = 2.9$ Hz, 1H), 6.76 (d, $J = 8.8$ Hz, 1H), 7.34 (d, $J = 8.5$ Hz, 1H), 7.51 (s, 1H), 8.46 (d, $J = 6.0$ Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 332 ($M^+ + 1$)

Production Example 4: 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylaniline

[0101] 4-Chloro-6,7-dimethoxyquinazoline (5.00 g) and 4-nitro-2-methylphenol (6.85 g) were suspended in monochlorobenzene (25 ml) to prepare a suspension which was then heated under reflux overnight. The solvent was removed by distillation under the reduced pressure. The residue was washed with ethyl acetate, was filtered, and was dried. Next, the resultant crystal was suspended in an aqueous sodium hydroxide solution to prepare a suspension. The suspension was then filtered, followed by drying to give 6.89 g of 4-(2-methyl-4-nitrophenoxy)-6,7-dimethoxyquinoline. 4-(2-Methyl-4-nitrophenoxy)-6,7-dimethoxyquinoline (1.36 g) was dissolved in ethyl acetate/ N,N -dimethylformamide/triethylamine (25 ml/25 ml/5 ml). Palladium hydroxide (0.4 g) was added to the solution, and the mixture was stirred in a hydrogen atmosphere at room temperature overnight. After filtration through Celite, the solvent was removed by distillation under the reduced pressure. A saturated aqueous sodium hydrogencarbonate solution was added to the residue, and the mixture was extracted with chloroform. The organic layer was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure to give the title compound (1.31 g, yield 91%).

Mass spectrometry value (ESI-MS, m/z): 311 ($M^+ + 1$)

Production Example 5: 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-methoxyaniline

[0102] Sodium hydride (60 wt%, 3.2 g) was added to dimethyl sulfoxide (50 ml), and the mixture was stirred at 50°C for 20 min. 4-Amino-3-methoxyphenol (5.6 g) was added thereto, and the mixture was stirred at room temperature for 10 min. Next, 4-chloro-6,7-dimethoxyquinazoline (7.0 g) was added thereto, and the mixture was stirred at 100°C overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The chloroform layer was then washed with a saturated aqueous sodium hydrogencarbonate solution and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. Methanol was added to the residue, and the precipitated crystal was collected by suction filtration to give the title compound (7.3 g, yield 72%).

Mass spectrometry value (ESI-MS, m/z) : 328 ($M^+ + 1$)

Example 1: 4-Methylbenzyl N-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0103] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (129 mg) was added to toluene/triethylamine = 10/1 (10 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (193 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methylbenzyl alcohol (79 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated, and the residue was purified on a column using chloroform/methanol to give the title compound (108 mg, yield 51%).

¹H-NMR (CDCl₃, 400 MHz): 8.61 (1H, s), 7.16 - 7.54 (10H, m), 6.70 (1H, s), 5.16 (2H, s), 4.05 (6H, s), 2.35 (3H, s)
Mass spectrometry value (ESI-MS, m/z) : 446 (M⁺+1)

Example 2: 4-Methylbenzyl N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0104] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)-oxy]aniline (109 mg) was added to toluene/triethylamine = 10/1 (10 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (146 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methylbenzyl alcohol (61 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (48 mg, yield 28%).

¹H-NMR (CDCl₃, 400 MHz): 8.61 (1H, s), 8.29 (1H, d, J = 9.0), 7.50 (1H, s), 7.15 - 7.35 (8H, m), 5.18 (2H, s), 4.05 (3H, s), 4.05 (3H, s), 2.36 (3H, s)
Mass spectrometry value (ESI-MS, m/z) : 481 (M⁺+1)

Example 3: 1-(3-Chlorophenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0105] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (72 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (109 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-chloro- α -methylbenzyl alcohol (46 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (88 mg, yield 70%).

¹H-NMR (CDCl₃, 400 MHz): 8.44 - 8.50 (1H, m), 8.14 (1H, s), 7.58 - 7.64 (3H, m), 7.26 - 7.42 (4H, m), 7.15 - 7.19 (2H, m), 6.86 (1H, s), 6.67 (1H, d, J = 6.6), 5.88 (1H, q, J = 6.6), 4.16

Example 4: 1-(3-Chlorophenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0106] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (75 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (100 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-chloro- α -methylbenzyl alcohol (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (62 mg, yield 49%).

¹H-NMR (CDCl₃, 400 MHz): 8.41 - 8.47 (1H, m), 8.15 (1H, s), 7.71 - 7.76 (1H, m), 7.66 (1H, s), 7.25 - 7.45 (4H, m), 7.01 (1H, d, J = 9.2 Hz), 6.50 - 6.55 (2H, m), 5.87 (1H, q, J = 6.5 Hz), 4.17 (3H, s), 4.11 (3H, s), 2.27 (3H, s), 2.10 (3H, s), 1.62 (3H, d, J = 6.5 Hz)

Mass spectrometry value (ESI-MS, m/z) : 508 (M⁺+1)

Example 5: 1-(3-Chlorophenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0107] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (75 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (110 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-chloro- α -methylbenzyl alcohol (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound

(70 mg, yield 56%).

¹H-NMR (CDCl₃, 400 MHz): 8.37 - 8.44 (1H, m), 8.07 (1H, s), 7.82 (1H, bs), 7.57 (1H, s), 7.34 (1H, s), 7.20 - 7.26 (3H, m), 6.88 (1H, s), 6.49 (1H, d, J = 6.6 Hz), 6.44 (1H, m), 5.80 (1H, q, J = 6.6 Hz), 4.10 (3H, s), 4.03 (3H, s), 2.22 (3H, s), 2.04 (3H, s), 1.56 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 508 (M⁺+1)

Example 6: 1-(3-Chlorophenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0108] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (72 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (100 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 15 min. Subsequently, 3-chloro- α -methylbenzyl alcohol (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (71 mg, yield 57%).

¹H-NMR (CDCl₃, 400 MHz) : 8.76 (1H, s), 8.07 (1H, s), 7.50 - 7.60 (3H, m), 7.15 - 7.39 (5H, m), 6.83 (1H, s), 6.75 - 6.78 (1H, m), 5.84 (1H, q, J = 6.8 Hz), 4.16 (3H, s), 4.09 (3H, s), 1.59 (3H, d, J = 6.8 Hz)

Mass spectrometry value (ESI-MS, m/z): 481 (M⁺+1)

Example 7: 1-(3-Chlorophenyl)ethyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0109] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (72 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (105 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-chloro- α -methylbenzyl alcohol (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (43 mg, yield 36%).

¹H-NMR (CDCl₃, 400 MHz): 8.77 (1H, s), 8.33 (1H, d, J = 9.0 Hz), 8.06 (1H, s), 7.55 (1H, s), 7.39 (1H, s), 7.22 - 7.32 (6H, m), 5.85 (1H, q, J = 6.7 Hz), 4.16 (3H, s), 4.09 (3H, s), 1.61 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 415 (M⁺+1)

Example 8: 4-Fluorobenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0110] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (72 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (108 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-fluorobenzyl alcohol (40 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (68 mg, yield 58%).

¹H-NMR (CDCl₃, 400 MHz): 8.44 - 8.50 (1H, m), 8.14 (1H, s), 7.63 (1H, s), 7.56 - 7.66 (2H, m), 7.38 - 7.44 (2H, m), 7.16 - 7.20 (2H, m), 7.05 - 7.11 (2H, m), 6.85 (1H, s), 6.68 (1H, s), 5.20 (2H, s), 4.17 (3H, s), 4.10 (3H, s)

Mass spectrometry value (ESI-MS, m/z) : 429 (M⁺+1)

Example 9: 4-Fluorobenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0111] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (78 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (110 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-fluorobenzyl alcohol (40 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1

N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (77 mg, yield 62%).

¹H-NMR (CDCl₃, 400 MHz) : 8.42 - 8.47 (1H, m), 8.16 (1H, s), 7.66 (1H, s), 6.99 - 7.45 (6H, m), 6.50 - 6.56 (2H, m), 5.20 (2H, s), 4.17 (3H, s), 4.11 (3H, s), 2.25 (3H, s), 2.10 (3H, s)

Mass spectrometry value (ESI-MS, m/z) : 477 (M⁺+1)

Example 10: 4-Fluorobenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0112] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (82 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (111 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-fluorobenzyl alcohol (40 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (88 mg, yield 68%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 - 8.48 (1H, m), 8.15 (1H, m), 7.91 (1H, s), 7.64 (1H, s), 6.94 - 7.53 (6H, m), 6.57 (1H, d, J = 6.6 Hz), 6.49 (1H, s), 5.20 (2H, s), 4.17 (3H, s), 4.11 (3H, s), 2.27 (3H, s), 2.13 (3H, s)

Mass spectrometry value (ESI-MS, m/z) : 477 (M⁺+1)

Example 11: 4-Fluorobenzyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0113] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (115 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 15 min. Subsequently, 4-fluorobenzyl alcohol (45 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (43 mg, yield 33%).

¹H-NMR (CDCl₃, 400 MHz) : 8.64 (1H, s), 7.56 (1H, s), 7.00 - 7.54 (9H, m), 6.72 (1H, s), 5.19 (2H, s), 4.09 (3H, s), 4.08 (3H, s)

Mass spectrometry value (ESI-MS, m/z) : 450 (M⁺+1)

Example 12: 4-Fluorobenzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0114] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (72 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (116 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 15 min. Subsequently, 4-fluorobenzyl alcohol (45 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (38 mg, yield 34%).

¹H-NMR (CDCl₃, 400 MHz) : 8.64 (1H, s), 8.30 (1H, d, J = 9.3 Hz), 7.52 (1H, s), 7.40 - 7.45 (3H, m), 7.32 - 7.34 (1H, m), 7.18 - 7.22 (2H, m), 7.06 - 7.12 (2H, m), 5.21 (2H, s), 4.08 (3H, s), 4.07 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 485 (M⁺+1)

Example 13: 1-(2-Chlorophenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0115] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (69 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (103 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 15 min. Subsequently, 2-chloro- α -methylbenzyl alcohol (55 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto.

The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (77 mg, yield 64%).

¹H-NMR (CDCl₃, 400 MHz): 8.40 - 8.48 (1H, m), 8.14 (1H, s), 7.15 - 7.64 (9H, m), 6.86 (1H, s), 6.67 (1H, d, J = 6.6 Hz), 6.28 (1H, q, J = 6.6 Hz), 4.16 (3H, s), 4.19 (3H, s), 1.63 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z) : 480 (M⁺+1)

Example 14: 1-(2-Chlorophenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0116] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (67 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (92 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 15 min. Subsequently, 2-chloro- α -methylbenzyl alcohol (48 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (88 mg, yield 79%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 (1H, d, J = 6.6 Hz), 8.14 (1H, s), 7.72 - 7.78 (1H, m), 7.66 (1H, s), 7.25 - 7.54 (4H, m), 7.00 (1H, d, J = 8.6 Hz), 6.50 - 6.57 (2H, m), 6.27 (1H, q, J = 6.6 Hz), 4.17 (3H, s), 4.11 (3H, s), 2.27 (3H, s), 2.09 (3H, s), 1.63 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 508 (M⁺+1)

Example 15: 1-(2-Chlorophenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0117] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (62 mg) was added to toluene/triethylamine = 10/1 (6 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (93 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 15 min. Subsequently, 2-chloro- α -methylbenzyl alcohol (49 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (52 mg, yield 48%).

Mass spectrometry value (ESI-MS, m/z): 480 (M⁺+1)

Example 16: 1-(2-Chlorophenyl)ethyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0118] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (61 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (91 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 15 min. Subsequently, 2-chloro- α -methylbenzyl alcohol (57 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (77 mg, yield 69%).

¹H-NMR (CDCl₃, 400 MHz): 8.77 (1H, s), 8.36 (1H, d, J = 8.8 Hz), 8.00 - 8.05 (1H, m), 7.16 - 7.57 (8H, m), 6.28 (1H, q, J = 6.8 Hz), 4.17 (3H, s), 4.10 (3H, s), 1.63 (3H, d, J = 6.8 Hz)

Mass spectrometry value (ESI-MS, m/z) : 515 (M⁺+1)

Example 17: 3-(2-Chlorophenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0119] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (78 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (117 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(2-chlorophenoxy)-1-propanol (67 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing

with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (80 mg, yield 58%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 (1H, d, J = 5.4 Hz), 7.61 (1H, s), 7.48 (1H, s), 7.35 - 7.40 (1H, m), 7.18 - 7.25 (2H, m), 6.87 - 7.05 (3H, m), 6.43 (1H, bs), 6.27 (1H, d, J = 4.9 Hz), 4.46 (2H, t, J = 6.2 Hz), 4.05 - 4.22 (2H, m), 4.07 (3H, s), 4.06 (3H, s), 2.24 (3H, s), 2.11 (3H, s), 2.10 - 2.22 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 538 (M⁺+1)

Example 18: 3-(2-Chlorophenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0120] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (71 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (97 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(2-chlorophenoxy)-1-propanol (72 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (62 mg, yield 44%).

¹H-NMR (CDCl₃, 400 MHz): 8.44 (1H, d, J = 5.4 Hz), 7.50 - 7.80 (2H, m), 7.19 - 7.40 (3H, m), 6.88 - 6.98 (3H, m), 6.35 - 6.48 (2H, m), 4.65 (2H, t, J = 6.2 Hz), 4.18 (2H, t, J = 6.0 Hz), 4.07 (3H, s), 4.07 (3H, s), 2.10 - 2.30 (8H, m)

Mass spectrometry value (ESI-MS, m/z): 538 (M⁺+1)

Example 19: 3-(2-Chlorophenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0121] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (77 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (115 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(2-chlorophenoxy)-1-propanol (72 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (62 mg, yield 44%).

¹H-NMR (CDCl₃, 400 MHz): 8.62 - 8.64 (1H, m), 7.55 - 7.57 (1H, m), 7.48 - 7.53 (2H, m), 7.35 - 7.40 (2H, m), 7.19 - 7.28 (3H, m), 6.87 - 6.97 (2H, m), 6.77 (1H, bs), 4.43 - 4.48 (2H, m), 4.14 - 4.20 (2H, m), 4.08 (3H, s), 4.07 (3H, s), 2.15 - 2.28 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 511 (M⁺+1)

Example 20: 3-(2-Chlorophenoxy)propyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0122] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-aniline (70 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (94 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(2-chlorophenoxy)-1-propanol (59 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (61 mg, yield 50%).

¹H-NMR (CDCl₃, 400 MHz): 8.63 (1H, s), 8.25 - 8.35 (1H, d), 7.52 (1H, s), 7.14 - 7.41 (6H, m), 6.88 - 6.98 (2H, m), 4.48 (2H, t, J = 6.2 Hz), 4.18 (2H, t, J = 6.2 Hz), 4.08 (3H, s), 4.07 (3H, s), 2.10 - 2.50 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 545 (M⁺+1)

Example 21: 4-(Trifluoromethyl)benzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0123] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (75 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (112 mg) in methylene chloride was

then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-trifluoromethylbenzyl alcohol (67 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (77 mg, yield 57%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 - 8.48 (1H, m), 8.14 (1H, s), 7.47 - 7.70 (7H, m), 7.15 - 7.22 (3H, m), 6.68 (1H, d, J = 6.6 Hz), 5.29 (2H, s), 4.16 (3H, s), 4.10 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 499 (M⁺+1)

Example 22: 4-(Trifluoromethyl)benzyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0124] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (77 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (105 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-trifluoromethylbenzyl alcohol (63 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (80 mg, yield 60%).

¹H-NMR (CDCl₃, 400 MHz): 8.44 (1H, d, J = 6.4 Hz), 8.00 - 8.15 (1H, m), 7.53 - 7.69 (6H, m), 7.03 (1H, d, J = 9.0 Hz), 6.54 - 6.65 (1H, m), 6.47 - 6.53 (1H, m), 5.29 (3H, s), 4.15 (3H, s), 4.11 (3H, s), 2.27 (3H, s), 2.11 (3H, s)

Mass spectrometry value (ESI-MS, m/z) : 528 (M⁺+1)

Example 23: 4-(Trifluoromethyl)benzyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0125] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (77 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (105 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-trifluoromethylbenzyl alcohol (63 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (80 mg, yield 48%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 - 8.48 (1H, m), 8.16 (1H, s), 7.50 - 7.95 (6H, m), 6.97 (1H, s), 6.55 - 6.60 (2H, m), 5.29 (2H, m), 4.17 (3H, s), 4.11 (3H, s), 2.29 (3H, s), 2.14 (3H, s)

Mass spectrometry value (ESI-MS, m/z) : 528 (M⁺+1)

Example 24: 4-(Trifluoromethyl)benzyl N-[4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl]carbamate

[0126] 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (70 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (105 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-trifluoromethylbenzyl alcohol (63 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (60 mg, yield 48%).

¹H-NMR (CDCl₃, 400 MHz): 8.70 (1H, s), 7.48 - 7.78 (8H, m), 7.20 - 7.24 (2H, m), 6.94 (1H, bs), 5.28 (2H, s), 4.13 (3H, s), 4.10 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 500 (M⁺+1)

Example 25: 4-(Trifluoromethyl)benzyl N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0127] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (74 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (99 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-trifluoromethylbenzyl alcohol (60 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (52 mg, yield 41%).

¹H-NMR (CDCl₃, 400 MHz): 8.62 - 8.65 (1H, m), 8.25 - 8.34 (1H, m), 7.16 - 7.71 (9H, m), 5.27 - 5.31 (2H, m), 4.05 - 4.08 (6H, m)

Mass spectrometry value (ESI-MS, m/z): 535 (M⁺+1)

Example 26: 3-(2-Chlorophenoxy)propyl N-[4-[(6,7-dimethoxy-4-quinolinyloxy)phenyl]carbamate

[0128] 4-[(6,7-Dimethoxy-4-quinolinyloxy)aniline (61 mg) was added to toluene/triethylamine = 10/1 (6 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (91 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(2-chlorophenoxy)-1-propanol (57 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (77 mg, yield 69%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 - 8.50 (1H, m), 8.15 (1H, s), 7.64 (1H, s), 7.56 - 7.65 (2H, m), 6.89 - 7.40 (6H, m), 6.81 (1H, s), 6.68 (1H, d, J = 6.4 Hz), 4.48 (2H, t, J = 6.2 Hz), 4.15 - 4.22 (2H, m), 4.17 (3H, s), 4.10 (3H, s), 2.20 - 2.30 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 510 (M⁺+1)

Example 27: 3-(4-Chlorophenoxy)propyl N-[4-[(6,7-dimethoxy-4-quinolinyloxy)phenyl]carbamate

[0129] 4-[(6,7-Dimethoxy-4-quinolinyloxy)aniline (79 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(4-chlorophenoxy)-1-propanol (60 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (80 mg, yield 55%).

¹H-NMR (CDCl₃, 400 MHz): 8.44 - 8.50 (1H, m), 8.15 (1H, s), 7.63 (1H, s), 7.52 - 7.64 (4H, m), 6.77 - 6.87 (3H, m), 6.68 (1H, d, J = 6.3 Hz), 4.41 (2H, t, J = 6.3 Hz), 4.17 (3H, s), 4.10 (3H, s), 4.05 - 4.10 (2H, m), 2.15 - 2.22 (2H, m)

Mass spectrometry value (ESI-MS, m/z) : 510 (M⁺+1)

Example 28: 3-(4-Chlorophenoxy)propyl N-[4-[(6,7-dimethoxy-4-quinolinyloxy)-2,3-dimethylphenyl]carbamate

[0130] 4-[(6,7-Dimethoxy-4-quinolinyloxy)-2,3-dimethylaniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (115 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(4-chlorophenoxy)-1-propanol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (84 mg, yield 60%).

¹H-NMR (CDCl₃, 400 MHz): 8.41 - 8.48 (1H, m), 8.16 (1H, s), 7.65 - 7.75 (1H, m), 6.82 - 7.27 (7H, m), 6.43 -

6.58 (1H, m), 4.41 (2H, d, J = 6.3 Hz), 4.17 (3H, s), 4.11 (3H, s), 4.05 - 4.15 (2H, m), 2.26 (3H, s), 2.10 (3H, s), 2.00 - 2.08 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 538 (M⁺+1)

Example 29: 3-(4-Chlorophenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0131] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (78 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (115 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(4-chlorophenoxy)-1-propanol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (71 mg, yield 51%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 - 8.48 (1H, m), 8.15 (1H, s), 7.88 (1H, bs), 7.64 (1H, s), 6.82 - 7.26 (6H, m), 6.57 (1H, d, J = 6.6 Hz), 6.43 (1H, bs), 4.12 (2H, t, J = 6.6 Hz), 4.17 (3H, s), 4.11 (3H, s), 4.05 - 4.11 (2H, m), 2.28 (3H, s), 2.15 - 2.23 (2H, m), 2.12 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 538 (M⁺+1)

Example 30: 3-(4-Chlorophenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinazolyl)oxy]phenyl}carbamate

[0132] 4-[(6,7-Dimethoxy-4-quinazolyl)oxy]aniline (78 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(4-chlorophenoxy)-1-propanol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (60 mg, yield 37%).

¹H-NMR (CDCl₃, 400 MHz): 8.79 (1H, s), 8.14 (1H, s), 7.61 (1H, s), 7.53 - 7.58 (2H, m), 7.16 - 7.26 (4H, m), 6.76 - 6.86 (3H, m), 4.40 (2H, t, J = 6.2 Hz), 4.19 (3H, s), 4.12 (3H, s), 4.02 - 4.10 (2H, m), 2.15 - 2.21 (2H, m)

Mass spectrometry value (ESI-MS, m/z) : 511 (M⁺+1)

Example 31: 3-(4-Chlorophenoxy)propyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolyl)oxy]phenyl}carbamate

[0133] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolyl)oxy]aniline (75 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (121 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(4-chlorophenoxy)-1-propanol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (58 mg, yield 44%).

¹H-NMR (CDCl₃, 400 MHz) : 8.70 (1H, s), 8.25 - 8.35 (1H, m), 7.65 - 7.70 (1H, m), 7.54 (1H, s), 7.15 - 7.35 (4H, m), 6.82 - 6.87 (3H, m), 4.42 (2H, t, J = 6.4 Hz), 4.12 (3H, s), 4.09 (3H, s), 4.05 - 4.13 (2H, m), 2.17 - 2.25 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 545 (M⁺+1)

Example 32: 1-(4-Methoxyphenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0134] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (73 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (110 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methoxy- α -methylbenzyl alcohol (56 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1

N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (74 mg, yield 59%).

¹H-NMR (CDCl₃, 400 MHz): 8.44 - 8.48 (1H, m), 8.14 (1H, s), 7.63 (1H, s), 7.55 - 7.62 (2H, m), 7.33 - 7.38 (2H, m), 7.14 - 7.18 (2H, m), 6.88 - 6.94 (2H, m), 6.79 (1H, s), 6.67 (1H, d, J = 6.4 Hz), 5.86 - 5.93 (1H, m), 4.16 (3H, s), 4.10 (3H, s), 3.82 (3H, s), 1.63 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 476 (M⁺+1)

Example 33: 1-(4-Methoxyphenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0135] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (68 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (94 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methoxy- α -methylbenzyl alcohol (48 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (75 mg, yield 66%).

¹H-NMR (CDCl₃, 400 MHz): 8.40 - 8.45 (1H, m), 8.15 (1H, s), 7.73 - 7.78 (1H, m), 7.66 (1H, s), 7.33 - 7.38 (2H, m), 6.98 - 7.02 (1H, m), 6.89 - 6.94 (2H, m), 6.53 (1H, d, J = 6.6 Hz), 6.46 (1H, bs), 5.85 - 5.92 (1H, m), 4.20 (3H, s), 4.11 (3H, s), 3.82 (3H, s), 2.24 (3H, s), 2.09 (3H, s), 1.63 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 504 (M⁺+1)

Example 34: 1-(4-Methoxyphenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0136] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (110 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methoxy- α -methylbenzyl alcohol (56 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (80 mg, yield 60%).

¹H-NMR (CDCl₃, 400 MHz): 8.41 - 8.47 (1H, m), 8.15 (1H, s), 7.92 (1H, s), 7.64 (1H, s), 6.80 - 7.40 (5H, m), 6.55 (1H, d, J = 6.6 Hz), 6.44 (1H, s), 5.85 - 5.92 (1H, m), 4.17 (3H, s), 4.11 (3H, s), 3.82 (3H, s), 2.26 (3H, s), 2.11 (3H, s), 1.64 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 504 (M⁺+1)

Example 35: 1-(4-Methoxyphenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}carbamate

[0137] 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (68 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (102 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methoxy- α -methylbenzyl alcohol (52 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (61 mg, yield 52%).

¹H-NMR (CDCl₃, 400 MHz): 8.72 (1H, s), 7.85 (1H, s like), 7.58 (1H, s), 7.48 - 7.55 (2H, m), 7.32 - 7.37 (2H, m), 7.15 - 7.20 (2H, m), 6.87 - 6.93 (2H, m), 6.72 (1H, s), 5.85 - 5.92 (1H, m), 4.14 (3H, s), 4.10 (3H, s), 3.81 (3H, s), 1.61 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 477 (M⁺+1)

Example 36: 1-(4-Methoxyphenyl)ethyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0138] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (66 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (88 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methoxy- α -methylbenzyl alcohol (45 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (58 mg, yield 53%).

¹H-NMR (CDCl₃, 400 MHz): 8.76 (1H, s like), 8.32 - 8.40 (1H, m), 6.88 - 8.00 (9H, m), 5.87 - 5.93 (1H, m), 4.16 (3H, s), 4.10 (3H, s), 3.82 (3H, s), 1.63 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z) : 511 (M⁺+1)

Example 37: 3-[(4-Methylphenyl)sulfanyl]propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0139] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (121 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-[(4-methylphenyl)sulfanyl]-1-propanol (74 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (98 mg, yield 67%).

¹H-NMR (CDCl₃, 400 MHz): 8.44 - 8.50 (H, m), 8.15 (1H, s), 7.64 (1H, s), 7.55 - 7.64 (2H, m), 7.10 - 7.31 (6H, m), 6.77 (1H, s), 6.69 (1H, d, J = 6.6 Hz), 4.32 (2H, t, J = 6.2 Hz), 4.17 (3H, s), 4.10 (3H, s), 2.97 - 3.03 (2H, m), 2.33 (3H, s), 1.95 - 2.05 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 506 (M⁺+1)

Example 38: 3-[(4-Methylphenyl)sulfanyl]propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0140] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethyl-aniline (85 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (122 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-[(4-methylphenyl)sulfanyl]-1-propanol (72 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (93 mg, yield 62%).

¹H-NMR (CDCl₃, 400 MHz) : 8.40 - 8.48 (1H, m), 8.16 (1H, s), 7.65 - 7.77 (2H, m), 7.00 - 7.31 (5H, m), 6.55 (1H, d, J = 6.4 Hz), 6.40 - 6.50 (1H, m), 4.29 - 4.40 (1H, m), 4.17 (3H, s), 4.11 (3H, s), 3.74 - 3.80 (1H, m), 2.95 - 3.05 (2H, m), 2.26 - 2.34 (6H, m), 2.10 (3H, s), 1.84 - 2.04 (2H, m)

Mass spectrometry value (ESI-MS, m/z) : 523 (M⁺+1)

Example 39: 3-[(4-Methylphenyl)sulfanyl]propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0141] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (85 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-[(4-methylphenyl)sulfanyl]-1-propanol (72 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (82 mg, yield 56%).

¹H-NMR (CDCl₃, 400 MHz): 8.40 - 8.49 (1H, m), 8.16 (1H, s), 7.85 - 7.92 (1H, m), 7.64 (1H, s), 7.08 - 7.32 (4H, m), 6.95 (1H, s), 6.57 (1H, d, J = 6.6 Hz), 6.40 (1H, s), 4.30 - 4.40 (2H, m), 4.17 (3H, s), 4.11 (3H, s), 2.95 - 3.15 (2H, m), 2.27 - 2.34 (6H, m), 2.13 (3H, s), 1.98 - 2.06 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 524 (M⁺+1)

Example 40: 3-[(4-Methylphenyl)sulfanyl]propyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)]phenyl}carbamate

[0142] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)]aniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-[(4-methylphenyl)sulfanyl]-1-propanol (74 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (82 mg, yield 56%).

¹H-NMR (CDCl₃, 400 MHz): 8.66 (1H, s), 7.57 (1H, s), 7.48 - 7.55 (2H, m), 7.10 - 7.31 (7H, m), 6.65 (1H, bs), 4.27 - 4.38 (2H, m), 4.10 (3H, s), 4.09 (3H, s), 2.95 - 3.15 (2H, m), 2.32 (3H, s), 1.95 - 2.05 (2H, m)

Mass spectrometry value (ESI-MS, m/z) : 507 (M⁺+1)

Example 41: 3-[(4-Methylphenyl)sulfanyl]propyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)]phenyl}carbamate

[0143] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)]aniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (125 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-[(4-methylphenyl)sulfanyl]-1-propanol (66 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (68 mg, yield 49%).

¹H-NMR (CDCl₃, 400 MHz) : 8.76 (1H, s), 8.31 - 8.38 (1H, m), 7.91 (1H, bs), 7.56 (2H, s), 7.10 - 7.34 (6H, m), 4.30 - 4.43 (2H, m), 4.16 (3H, s), 4.11 (3H, s), 3.00 (2H, t, J = 7.0 Hz), 2.32 (3H, s), 1.97 - 2.06 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 541 (M⁺+1)

Example 42: 3-(4-Methoxyphenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolinyloxy)]phenyl}carbamate

[0144] 4-[(6,7-Dimethoxy-4-quinolinyloxy)]aniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(4-methoxyphenoxy)-1-propanol (73 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (118 mg, yield 80%).

¹H-NMR (CDCl₃, 400 MHz): 8.44 - 8.48 (1H, m), 8.14 (1H, s), 7.64 (1H, s), 7.57 - 7.64 (2H, m), 7.15 - 7.20 (2H, m), 6.83 - 6.87 (5H, m), 6.65 - 6.72 (1H, m), 4.17 (3H, s), 4.10 (3H, s), 4.42 (2H, t, J = 6.2 Hz), 4.06 (2H, t, J = 6.2 Hz), 3.77 (3H, s), 2.17 (2H, t, J = 6.2 Hz)

Mass spectrometry value (ESI-MS, m/z): 506 (M⁺+1)

Example 43: 3-(4-Methoxyphenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolinyloxy)]-2,3-dimethylphenyl}carbamate

[0145] 4-[(6,7-Dimethoxy-4-quinolinyloxy)]-2,3-dimethylaniline (88 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (122 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(4-methoxyphenoxy)-1-propanol (74 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled

water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (128 mg, yield 83%).

¹H-NMR (CDCl₃, 400 MHz): 8.42 - 8.46 (1H, m), 8.16 (1H, s), 7.66 - 7.75 (1H, m), 7.02 (1H, d, J = 8.8 Hz), 6.80 - 6.87 (5H, m), 6.55 (1H, d, J = 6.6 Hz), 6.46 (1H, bs), 4.41 (2H, t, J = 6.4 Hz), 4.17 (3H, s), 4.11 (3H, s), 4.04 - 4.10 (2H, m), 3.77 (3H, s), 2.26 (3H, s), 2.10 (3H, s), 2.14 - 2.21 (2H, m)

Mass spectrometry value (ESI-MS, m/z) : 534 (M⁺+1)

Example 44: 3-(4-Methoxyphenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0146] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (98 mg) was added to toluene/triethylamine = 10/1 (10 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (136 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(4-methoxyphenoxy)-1-propanol (83 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (130 mg, yield 76%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 - 8.47 (1H, m), 8.15 (1H, s), 7.89 (1H, bs), 7.64 (1H, s), 6.80 - 6.97 (5H, m), 6.57 (1H, d, J = 6.6 Hz), 6.44 (1H, s), 4.42 (2H, t, J = 6.3 Hz), 4.17 (3H, s), 4.11 (3H, s), 4.06 (2H, t, J = 6.3 Hz), 3.77 (3H, s), 2.28 (3H, s), 2.14 - 2.24 (2H, m), 2.12 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 534 (M⁺+1)

Example 45: 3-(4-Methoxyphenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0147] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (82 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (122 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(4-methoxyphenoxy)-1-propanol (75 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (92 mg, yield 62%).

¹H-NMR (CDCl₃, 400 MHz): 8.66 (1H, s), 7.57 (1H, s), 7.40 - 7.54 (3H, m), 7.18 - 7.24 (2H, m), 6.65 - 6.85 (5H, m), 4.40 (2H, t, J = 6.3 Hz), 4.09 (3H, s), 4.08 (3H, s), 4.05 (2H, t, J = 6.1 Hz), 3.77 (3H, s), 2.10 - 2.20 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 507 (M⁺+1)

Example 46: 3-(4-Methoxyphenoxy)propyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0148] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (87 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (117 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(4-methoxyphenoxy)-1-propanol (72 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (68 mg, yield 45%).

¹H-NMR (CDCl₃, 400 MHz): 8.68 (1H, s), 8.30 (1H, d, J = 8.5 Hz), 7.53 - 7.60 (2H, m), 6.80 - 7.34 (7H, m), 4.42 (2H, t, J = 6.4 Hz), 4.11 (3H, s), 4.08 (3H, s), 4.06 (2H, t, J = 6.2 Hz), 3.77 (3H, s), 2.15 - 2.22 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 540 (M⁺+1)

Example 47: 3-(3-Methoxyphenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0149] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (75 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the

mixture was heated under reflux to prepare a solution. A solution of triphosgene (112 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(3-methoxyphenoxy)-1-propanol (69 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (88 mg, yield 69%).

¹H-NMR (CDCl₃, 400 MHz): 8.45 - 8.51 (1H, m), 8.14 (1H, s), 7.63 (1H, s), 7.54 - 7.64 (2H, m), 7.15 - 7.23 (3H, m), 6.82 (1H, s), 6.69 (1H, d, J = 6.6 Hz), 6.45 - 6.55 (3H, m), 4.42 (2H, t, J = 6.2 Hz), 4.17 (3H, s), 4.10 (3H, s), 4.09 (2H, t, J = 6.1 Hz), 3.79 (3H, s), 2.15 - 2.22 (2H, m)

Mass spectrometry value (ESI-MS, m/z) : 506 (M⁺+1)

Example 48: 3-(3-Methoxyphenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0150] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethyl-aniline (85 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (116 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(3-methoxyphenoxy)-1-propanol (72 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (91 mg, yield 72%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 (1H, d, J = 5.4 Hz), 7.50 - 7.63 (2H, m), 6.28 - 7.24 (8H, m), 4.40 (2H, t, J = 6.3 Hz), 4.07 (6H, s), 4.05 - 4.10 (2H, m), 3.79 (3H, s), 2.24 (3H, s), 2.15 - 2.23 (2H, m), 2.11 (3H, s)

Mass spectrometry value (ESI-MS, m/z) : 534 (M⁺+1)

Example 49: 3-(3-Methoxyphenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0151] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (77 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (105 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(3-methoxyphenoxy)-1-propanol (65 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (91 mg, yield 72%).

¹H-NMR (CDCl₃, 400 MHz): 8.40 - 8.48 (1H, m), 8.15 (1H, s), 7.89 (1H, s), 8.63 - 8.68 (1H, m), 6.93 - 7.25 (2H, m), 6.40 - 6.59 (5H, m), 4.38 - 4.45 (2H, m), 4.17 (3H, s), 4.11 (3H, s), 4.05 - 4.14 (2H, m), 3.79 (3H, s), 2.15 - 2.25 (2H, m), 2.28 (3H, s), 2.12 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 534 (M⁺+1)

Example 50: 3-(3-Methoxyphenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0152] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (95 mg) was added to toluene/triethylamine = 10/1 (10 ml), and the mixture was then added to the solution, and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (142 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(3-methoxyphenoxy)-1-propanol (87 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (105 mg, yield 65%).

¹H-NMR (CDCl₃, 400 MHz): 8.69 (1H, s), 7.45 - 7.97 (3H, m), 7.13 - 7.21 (3H, m), 6.40 - 6.80 (5H, m), 4.38 (2H, t, J = 6.4 Hz), 4.10 (3H, s), 4.07 (3H, s), 3.98 - 4.08 (2H, m), 3.77 (3H, s), 2.08 - 2.20 (2H, m)

Mass spectrometry value (ESI-MS, m/z) : 507 (M⁺+1)

Example 51: 3-(3-Methoxyphenoxy)propyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}carbamate

[0153] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (107 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(3-methoxyphenoxy)-1-propanol (67 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (67 mg, yield 52%)

¹H-NMR (CDCl₃, 400MHz): 8.70 (1H, s), 8.31 (1H, d, J = 9.0 Hz), 7.54 (1H, s), 7.33 (1H, d, J = 2.7 Hz), 7.15 - 7.23 (3H, m), 6.47 - 6.55 (4H, m), 4.43 (2H, t, J = 6.2 Hz), 4.12 (3H, s), 4.09 (3H, s), 4.08 - 4.13 (2H, m), 3.79 (3H, s), 2.15 - 2.25 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 541 (M⁺+1)

Example 52: 1-(3-Methoxyphenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0154] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (83 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (124 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-methoxy- α -methylbenzyl alcohol (64 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (88 mg, yield 66%).

¹H-NMR (CDCl₃, 400 MHz): 8.46 (1H, dd, J = 6.5 Hz), 8.14 (1H, s), 7.58 - 7.64 (2H, m), 7.38 - 7.42 (1H, m), 7.29 - 7.32 (1H, m), 7.14 - 7.18 (2H, m), 6.96 - 7.02 (1H, m), 6.91 (1H, d, J = 8.3 Hz), 6.86 (1H, s), 6.68 (1H, d, J = 6.6 Hz), 6.29 (1H, q, J = 6.5 Hz), 4.16 (3H, s), 4.10 (3H, s), 3.88 (3H, s), 1.58 (3H, d, J = 6.5 Hz)

Mass spectrometry value (ESI-MS, m/z): 476 (M⁺+1)

Example 53: 1-(3-Methoxyphenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0155] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (90 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (123 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-methoxy- α -methylbenzyl alcohol (64 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (97 mg, yield 70%).

¹H-NMR (CDCl₃, 400 MHz): 8.41 - 8.46 (1H, m), 8.15 (1H, s), 7.77 (1H, d, J = 8.6 Hz), 7.66 (1H, s), 7.40 (1H, d, J = 7.8 Hz), 7.30 (1H, d, J = 7.3 Hz), 6.96 - 7.20 (2H, m), 6.91 (1H, d, J = 8.3 Hz), 6.50 - 6.55 (2H, m), 6.29 (1H, q, J = 6.5 Hz), 4.17 (3H, s), 4.11 (3H, s), 3.87 (3H, s), 2.27 (3H, s), 2.09 (3H, s), 1.59 (3H, d, J = 6.5 Hz)

Mass spectrometry value (ESI-MS, m/z): 504 (M⁺+1)

Example 54: 1-(3-Methoxyphenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0156] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (90 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (123 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-methoxy- α -methylbenzyl alcohol (64 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound

(78 mg, yield 56%).

¹H-NMR (CDCl₃, 400 MHz): 8.41 - 8.48 (1H, m), 8.12 (1H, s), 7.92 (1H, s), 7.62 (1H, s), 7.26 - 7.42 (2H, m), 6.85 - 7.00 (3H, m), 6.45 - 6.58 (2H, m), 6.27 (1H, q, J = 6.5 Hz), 4.14 (3H, s), 4.08 (3H, s), 3.86 (3H, s), 2.27 (3H, s), 2.08 (3H, s), 1.57 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 504 (M⁺+1)

Example 55: 1-(3-Methoxyphenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0157] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (83 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (124 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-methoxy- α -methylbenzyl alcohol (64 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (76 mg, yield 58%).

¹H-NMR (CDCl₃, 400 MHz): 8.75 (1H, s), 8.00 (1H, bs), 7.16 - 7.62 (7H, m), 6.88 - 7.02 (2H, m), 6.79 (1H, bs), 6.28 (1H, q, J = 6.4 Hz), 4.16 (3H, s), 4.11 (3H, s), 3.87 (3H, s), 1.58 (3H, d, J = 6.4 Hz)

Mass spectrometry value (ESI-MS, m/z): 477 (M⁺+1)

Example 56: 1-(3-Methoxyphenyl)ethyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0158] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (82 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (110 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-methoxy- α -methylbenzyl alcohol (56 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (69 mg, yield 55%).

¹H-NMR (CDCl₃, 400 MHz) : 8.80 (1H, s), 8.40 (1H, d, J = 9.0 Hz), 8.14 (1H, s), 7.14 - 7.60 (5H, m), 6.97 - 7.03 (1H, m), 6.91 (1H, d, J = 8.3 Hz), 6.30 (1H, q, J = 6.5 Hz), 4.19 (3H, s), 4.12 (3H, s), 3.88 (3H, s), 1.60 (3H, d, J = 6.5 Hz)

Mass spectrometry value (ESI-MS, m/z): 511 (M⁺+1)

Example 57: 4-(Tert-butyl)benzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0159] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (90 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (137 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methoxy-tert-butylbenzyl alcohol (75 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (109 mg, yield 69%).

¹H-NMR (CDCl₃, 400 MHz): 8.46 (1H, dd, J = 6.7 Hz), 8.15 (1H, s), 7.64 (1H, s), 7.59 (2H, d, J = 9.0 Hz), 7.43 (2H, d, J = 9.0 Hz), 7.36 (2H, d, J = 8.3 Hz), 7.18 (2H, d, J = 9.0 Hz), 6.82 (1H, s), 6.68 (1H, d, J = 6.7 Hz), 5.21 (2H, s), 4.17 (3H, s), 4.19 (3H, s), 1.34 (9H, s)

Mass spectrometry value (ESI-MS, m/z): 488 (M⁺+1)

Example 58: 4-(Tert-butyl)benzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0160] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (83 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (115 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methoxy-tert-butylbenzyl alcohol (63 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2

hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (101 mg, yield 72%).

¹H-NMR (CDCl₃, 400 MHz): 8.42 - 8.47 (1H, m), 8.16 (1H, s), 7.75 - 7.85 (1H, m), 7.67 (1H, s), 7.44 (2H, d, J = 8.6 Hz), 7.38 (2H, d, J = 8.3 Hz), 7.03 (1H, d, J = 9.0 Hz), 6.55 (1H, d, J = 6.6 Hz), 6.52 (1H, bs), 5.21 (2H, s), 4.17 (3H, s), 4.11 (3H, s), 2.25 (3H, s), 2.09 (3H, s), 1.34 (9H, s)

Mass spectrometry value (ESI-MS, m/z) : 516 (M⁺+1)

Example 59: 4-(Tert-butyl)benzyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0161] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (111 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methoxy-tert-butylbenzyl alcohol (61 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (93 mg, yield 68%).

¹H-NMR (CDCl₃, 400 MHz): 8.40 - 8.47 (1H, m), 8.15 (1H, s), 7.95 (1H, bs), 7.64 (1H, s), 7.36 - 7.46 (4H, m), 6.95 (1H, s), 6.57 (1H, d, J = 6.6 Hz), 6.50 (1H, s), 5.21 (2H, s), 4.17 (3H, s), 4.11 (3H, s), 2.26 (3H, s), 2.13 (3H, s), 1.34 (9H, s)

Mass spectrometry value (ESI-MS, m/z) : 516 (M⁺+1)

Example 60: 4-(Tert-butyl)benzyl N-[4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl]carbamate

[0162] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (95 mg) was added to toluene/triethylamine = 10/1 (10 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (144 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methoxy-tert-butylbenzyl alcohol (79 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (71 mg, yield 42%).

¹H-NMR (CDCl₃, 400 MHz): 8.77 (1H, s), 8.07 (1H, bs), 7.61 (1H, s), 7.51 - 7.58 (2H, m), 7.42 (2H, d, J = 8.6 Hz), 7.36 (2H, d, J = 8.3 Hz), 7.19 (2H, d, J = 9.0 Hz), 6.79 (1H, s), 5.20 (2H, s), 4.18 (3H, s), 4.12 (3H, s), 1.33 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 489 (M⁺+1)

Example 61: 4-(Tert-butyl)benzyl N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl]carbamate

[0163] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (90 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (122 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methoxy-tert-butylbenzyl alcohol (67 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (55 mg, yield 36%).

¹H-NMR (CDCl₃, 400 MHz): 8.80 (1H, s), 8.41 (1H, d, J = 9.2 Hz), 8.13 (1H, s), 7.58 (1H, s), 7.36 - 7.46 (4H, m), 7.24 - 7.34 (2H, m), 7.17 - 7.22 (1H, m), 5.22 (2H, s), 4.19 (3H, s), 4.12 (3H, s), 1.34 (9H, s)

Mass spectrometry value (ESI-MS, m/z): 523 (M⁺+1)

Example 62: 3,4-Dimethoxybenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0164] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (65 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (100 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3,4-dimethoxybenzyl alcohol (55 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (70 mg, yield 60%).

¹H-NMR (CDCl₃, 400 MHz): 8.49 (1H, s), 8.14 (1H, s), 7.58 - 7.64 (3H, m), 7.17 - 7.22 (2H, m), 6.86 - 7.04 (4H, m), 6.69 (1H, m), 5.17 (2H, s), 4.17 (3H, s), 4.10 (3H, s), 3.92 (3H, s), 3.90 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

Example 63: 3,4-Dimethoxybenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0165] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (65 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (107 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3,4-dimethoxybenzyl alcohol (60 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (73 mg, yield 55%).

¹H-NMR (CDCl₃, 400 MHz): 8.46 (1H, dd, J = 6.6 Hz), 8.15 (1H, s), 7.75 - 7.80 (1H, m), 7.66 (1H, s), 6.83 - 7.05 (4H, m), 6.55 (1H, d, J = 6.4 Hz), 6.51 (1H, s), 5.17 (2H, s), 4.17 (3H, s), 4.12 (3H, s), 3.92 (3H, s), 3.91 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 520 (M⁺+1)

Example 64: 3,4-Dimethoxybenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0166] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (89 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (124 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3,4-dimethoxybenzyl alcohol (72 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (102 mg, yield 67%).

¹H-NMR (CDCl₃, 400 MHz): 8.44 - 8.50 (1H, m), 8.12 (1H, s), 7.91 (1H, s), 7.62 (1H, s), 6.80 - 7.03 (4H, m), 6.55 (1H, d, J = 6.3 Hz), 6.48 (1H, s), 5.15 (2H, s), 4.15 (3H, s), 4.08 (3H, s), 3.90 (3H, s), 3.88 (3H, s), 2.24 (3H, s), 2.11 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 519 (M⁺+1)

Example 65: 3,4-Dimethoxybenzyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}carbamate

[0167] 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (83 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (147 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3,4-dimethoxybenzyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (70 mg, yield 48%).

¹H-NMR (CDCl₃, 400 MHz): 8.79 (1H, s), 8.14 (1H, s), 7.54 - 7.64 (3H, m), 7.18 - 7.24 (2H, m), 6.79 - 7.01 (4H, m), 5.16 (2H, s), 4.19 (3H, s), 4.12 (3H, s), 3.92 (3H, s), 3.90 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

Example 66: 3,4-Dimethoxybenzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0168] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (76 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (105 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3,4-dimethoxybenzyl alcohol (58 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (53 mg, yield 42%).

¹H-NMR (CDCl₃, 400 MHz): 8.68 (1H, s), 8.33 (1H, d, J = 8.8 Hz), 7.50 - 7.60 (2H, m), 6.83 - 7.35 (6H, m), 5.18 (2H, s), 4.11 (3H, s), 4.08 (3H, s), 3.93 (3H, s), 3.90 (3H, s)

Mass spectrometry value (ESI-MS, m/z) : 527 (M⁺+1)

Example 67: 2,5-Dimethoxybenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0169] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (75 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3,5-dimethoxybenzyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (90 mg, yield 68%).

¹H-NMR (CDCl₃, 400 MHz): 8.47 (1H, d like, J = 6.6 Hz), 8.14 (1H, s), 6.67 - 7.66 (10H, m), 5.27 (2H, s), 4.17 (3H, s), 4.10 (3H, s), 3.84 (3H, s), 3.79 (3H, s)

Mass spectrometry value (ESI-MS, m/z) : 491 (M⁺+1)

Example 68: 2,5-Dimethoxybenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0170] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (85 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3,5-dimethoxybenzyl alcohol (80 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (92 mg, yield 60%).

¹H-NMR (CDCl₃, 400 MHz): 8.44 (1H, d, J = 6.4 Hz), 8.05 (1H, s), 7.74 - 7.80 (1H, m), 7.66 (1H, s), 6.78 - 7.40 (4H, m), 6.50 - 6.58 (2H, m), 5.27 (2H, s), 4.16 (3H, s), 4.11 (3H, s), 3.85 (3H, s), 3.79 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 520 (M⁺+1)

Example 69: 2,5-Dimethoxybenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0171] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (90 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (125 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3,5-dimethoxybenzyl alcohol (73 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (92 mg, yield 60%).

¹H-NMR (CDCl₃, 400 MHz): 8.46 (1H, d like, J = 6.6 Hz), 8.15 (1H, s), 7.95 (1H, s), 7.65 (1H, s), 6.85 - 7.02 (4H, m), 6.58 (1H, d, J = 6.6 Hz), 6.53 (2H, s), 5.28 (2H, s), 4.17 (3H, s), 4.11 (3H, s), 3.85 (3H, s), 3.80 (3H, s)
Mass spectrometry value (ESI-MS, m/z) : 519 (M⁺+1)

5 Example 70: 2,5-Dimethoxybenzyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0172] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (72 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3,5-dimethoxybenzyl alcohol (65 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (66 mg, yield 52%).

¹H-NMR (CDCl₃, 400 MHz): 8.80 (1H, s), 8.14 (1H, s), 7.55 - 7.63 (3H, m), 7.16 - 7.22 (2H, m), 6.83 - 7.00 (3H, m), 5.26 (2H, s), 4.19 (3H, s), 4.12 (3H, s), 3.83 (3H, s), 3.79 (3H, s)
Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

20 Example 71: 2,5-Dimethoxybenzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0173] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (76 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (105 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3,5-dimethoxybenzyl alcohol (60 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (59 mg, yield 46%).

¹H-NMR (CDCl₃, 400 MHz): 8.75 (1H, s), 8.39 (1H, d, J = 9.3 Hz), 6.73 - 7.85 (8H, m), 5.28 (2H, s), 4.15 (3H, s), 4.10 (3H, s), 3.84 (3H, s), 3.80 (3H, s)
Mass spectrometry value (ESI-MS, m/z): 527 (M⁺+1)

35 Example 72: 3-[[4-(Tert-butyl)phenyl]sulfanyl]propyl N-{4-[(6,7-dimethoxy-4-quinolinyloxy)phenyl]carbamate

[0174] 4-[(6,7-Dimethoxy-4-quinolinyloxy)aniline (72 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-[4-(tert-butyl)phenyl]sulfanyl-1-propanol (80 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (81 mg, yield 57%).

¹H-NMR (CDCl₃, 400 MHz): 8.45 - 8.50 (1H, m), 8.14 (1H, s), 7.64 (1H, s), 7.58 - 7.66 (2H, m), 7.16 - 7.33 (6H, m), 6.80 (1H, s), 6.69 (1H, d, J = 6.6 Hz), 4.33 (2H, t, J = 6.2 Hz), 4.17 (3H, s), 4.10 (3H, s), 3.01 (2H, t, J = 7.2 Hz), 1.99 - 2.07 (2H, m), 1.31 (9H, s)

Mass spectrometry value (ESI-MS, m/z): 548 (M⁺+1)

50 Example 73: 3-[[4-(Tert-butyl)phenyl]sulfanyl]propyl N-{4-[(6,7-dimethoxy-4-quinolinyloxy)-2,3-dimethylphenyl]carbamate

[0175] 4-[(6,7-Dimethoxy-4-quinolinyloxy)-2,3-dimethylaniline (78 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (121 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-[4-(tert-butyl)phenyl]sulfanyl-1-propanol (80 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before

distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (109 mg, yield 74%).

¹H-NMR (CDCl₃, 400 MHz): 8.44 (1H, d, J = 5.4 Hz), 7.48 - 7.64 (3H, m), 7.27 - 7.35 (4H, m), 6.97 - 7.03 (1H, m), 6.38 (1H, bs), 6.28 (1H, d, J = 5.4 Hz), 4.31 (2H, t, J = 6.2 Hz), 4.07 (3H, s), 2.98 - 3.13 (2H, m), 2.25 (3H, s), 2.12 (3H, s), 1.98 - 2.06 (2H, m), 1.30 (9H, s)

Mass spectrometry value (ESI-MS, m/z): 576 (M⁺+1)

Example 74: 3-[[4-(Tert-butyl)phenyl]sulfanyl]propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl} carbamate

[0176] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (82 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (122 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-[4-(tert-butyl)phenyl]sulfanyl-1-propanol (80 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (113 mg, yield 73%).

¹H-NMR (CDCl₃, 400 MHz): 8.45 - 8.50 (1H, m), 8.15 (1H, s), 7.89 (1H, s), 7.65 (1H, s), 7.32 (4H, s), 6.95 (1H, s), 6.58 (1H, d, J = 6.4 Hz), 6.44 (1H, s), 4.33 (2H, t, J = 6.4 Hz), 4.17 (3H, s), 4.11 (3H, s), 3.02 (2H, t, J = 7.1 Hz), 2.29 (3H, s), 2.13 (3H, s), 2.00 - 2.08 (2H, m), 1.31 (9H, s)

Mass spectrometry value (ESI-MS, m/z): 576 (M⁺+1)

Example 75: 3-[[4-(Tert-butyl)phenyl]sulfanyl]propyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}carbamate

[0177] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-[4-(tert-butyl)phenyl]sulfanyl-1-propanol (80 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (100 mg, yield 64%).

¹H-NMR (CDCl₃, 400 MHz): 8.73 (1H, s like), 8.52 - 8.60 (1H, m), 7.70 - 7.90 (2H, m), 6.80 - 7.65 (8H, m), 4.29 - 4.33 (2H, m), 4.10 - 4.16 (6H, m), 2.98 - 3.04 (2H, m), 1.90 - 2.10 (2H, m), 1.31 (9H, s)

Mass spectrometry value (ESI-MS, m/z): 549 (M⁺+1)

Example 76: 3-[[4-(Tert-butyl)phenyl]sulfanyl]propyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl} carbamate

[0178] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (77 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (125 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-[4-(tert-butyl)phenyl]sulfanyl-1-propanol (80 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (68 mg, yield 47%).

¹H-NMR (CDCl₃, 400 MHz): 8.80 (1H, s), 8.33 - 8.38 (1H, m), 8.07 (1H, bs), 7.15 - 7.62 (8H, m), 4.35 (2H, t, J = 6.2 Hz), 4.18 (3H, s), 4.12 (3H, s), 3.02 (2H, t, J = 7.1 Hz), 2.00 - 2.08 (2H, m), 1.31 (9H, s)

Mass spectrometry value (ESI-MS, m/z): 583 (M⁺+1)

Example 77: 3-[(4-Chloro-2-methylphenyl)sulfanyl]propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0179] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (73 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-[4-chloro-2-methylphenyl]sulfanyl-1-propanol (80 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (98 mg, yield 69%).

¹H-NMR (CDCl₃, 400 MHz): 8.45 - 8.50 (1H, m), 8.15 (1H, s), 7.57 - 7.65 (3H, m), 7.12 - 7.25 (5H, m), 6.82 (1H, s), 6.69 (1H, d, J = 6.6 Hz), 4.33 (2H, t, J = 6.2 Hz), 4.17 (3H, s), 4.10 (3H, s), 2.99 (2H, t, J = 7.2 Hz), 2.37 (3H, s), 1.95 - 2.08 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 540 (M⁺+1)

Example 78: 3-[(4-Chloro-2-methylphenyl)sulfanyl]propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0180] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (82 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-[4-chloro-2-methylphenyl]sulfanyl-1-propanol (80 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (88 mg, yield 58%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 - 8.50 (1H, m), 8.16 (1H, s), 7.66 - 7.76 (2H, m), 7.00 - 7.25 (5H, m), 6.55 (1H, d, J = 6.6 Hz), 6.46 (1H, s), 4.33 (2H, t, J = 6.2 Hz), 4.17 (3H, s), 4.11 (3H, s), 2.96 - 3.03 (2H, m), 2.37 (3H, s), 2.27 (3H, s), 2.11 (3H, s), 1.98 - 2.10 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 468 (M⁺+1)

Example 79: 3-[(4-Chloro-2-methylphenyl)sulfanyl]propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0181] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (90 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-[4-chloro-2-methylphenyl]sulfanyl-1-propanol (80 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (81 mg, yield 49%).

¹H-NMR (CDCl₃, 400 MHz): 8.42 - 8.48 (1H, m), 8.12 (1H, s), 7.86 (1H, s), 7.62 (1H, s), 7.08 - 7.23 (3H, m), 6.94 (1H, s), 6.56 (1H, d, J = 6.6 Hz), 6.43 (1H, s), 4.31 (2H, t, J = 6.2 Hz), 4.15 (3H, s), 4.08 (3H, s), 2.97 (2H, t, J = 7.2 Hz), 2.35 (3H, s), 2.26 (3H, s), 2.11 (3H, s), 1.96 - 2.06 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 568 (M⁺+1)

Example 80: 3-[(4-Chloro-2-methylphenyl)sulfanyl]propyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}carbamate

[0182] 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (88 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-[4-chloro-2-methylphenyl]sulfanyl-1-propanol (80 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by

washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (77 mg, yield 45%).

¹H-NMR (CDCl₃, 400 MHz): 8.73 (1H, s), 7.85 (1H, bs), 7.60 (1H, s), 7.51 - 7.57 (2H, m), 7.10 - 7.24 (5H, m), 6.74 (5H, m), 4.32 (2H, t, J = 6.1 Hz), 4.15 (3H, s), 4.11 (3H, s), 2.98 (2H, t, J = 7.2 Hz), 2.37 (3H, s), 1.98 - 2.07 (2H, m)
Mass spectrometry value (ESI-MS, m/z): 541 (M⁺+1)

Example 81: 3-[(4-Chloro-2-methylphenyl)sulfanyl]propyl N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl] carbamate

[0183] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (75 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-[4-chloro-2-methylphenyl]sulfanyl-1-propanol (80 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (69 mg, yield 50%).

¹H-NMR (CDCl₃, 400 MHz): 8.66 (1H, s), 8.23 - 8.33 (1H, m), 7.53 (1H, s), 7.46 (1H, s), 7.34 (1H, d, J = 2.7 Hz), 7.12 - 7.25 (5H, m), 4.34 (2H, t, J = 7.1 Hz), 4.09 (3H, s), 4.08 (3H, s), 3.00 (2H, t, J = 7.1 Hz), 2.37 (3H, s), 2.00 - 2.08 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 575 (M⁺+1)

Example 82: 3-(Trifluoromethyl)phenethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]carbamate

[0184] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (72 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (125 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-trifluoromethylphenethyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (101 mg, yield 76%).

¹H-NMR (CDCl₃, 400 MHz): 8.42 - 8.49 (1H, m), 8.12 (1H, s), 7.61 (1H, s), 7.42 - 7.59 (6H, m), 7.13 - 7.18 (2H, m), 6.76 (1H, s), 6.66 (1H, d, J = 6.6 Hz), 4.44 (2H, t, J = 6.7 Hz), 4.15 (3H, s), 4.08 (3H, s), 3.07 (2H, t, J = 6.7 Hz)

Mass spectrometry value (ESI-MS, m/z): 513 (M⁺+1)

Example 83: 3-(Trifluoromethyl)phenethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0185] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (68 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (125 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-trifluoromethylphenethyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (88 mg, yield 73%).

¹H-NMR (CDCl₃, 400 MHz): 8.4 - 8.49 (1H, m), 8.16 (1H, s), 7.67 (1H, s), 7.40 - 7.56 (5H, m), 7.02 (1H, d, J = 8.8 Hz), 6.54 (1H, d, J = 6.4 Hz), 6.42 (1H, bs), 4.46 (2H, t, J = 6.7 Hz), 4.17 (3H, s), 4.11 (3H, s), 3.09 (2H, t, J = 6.7 Hz), 2.23 (3H, s), 2.10 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 541 (M⁺+1)

Example 84: 3-(Trifluoromethyl)phenethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0186] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (80 mg) was added to toluene/triethylamine = 10/1 (8

ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (125 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-trifluoromethylphenethyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (79 mg, yield 56%).

¹H-NMR (CDCl₃, 400 MHz): 8.13 - 8.62 (2H, m), 7.26 - 8.00 (6H, m), 6.96 (1H, s), 6.64 - 6.28 (1H, m), 6.42 (1H, bs), 4.46 (2H, t, J = 6.7 Hz), 4.03 - 4.18 (6H, m), 3.07 - 3.13 (3H, m), 2.23 - 2.30 (3H, m), 2.11 (3H, s)

Mass spectrometry value (ESI-MS, m/z) : 541 (M⁺+1)

Example 85: 3-(Trifluoromethyl)phenethyl N-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0187] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (82 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (125 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-trifluoromethylphenethyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (68 mg, yield 45%).

¹H-NMR (CDCl₃, 400 MHz): 8.76 (1H, s), 8.01 (1H, s), 7.60 (1H, s), 7.43 - 7.58 (6H, m), 7.17 - 7.24 (2H, m), 6.79 (1H, s), 4.44 (2H, t, J = 6.7 Hz), 4.17 (3H, s), 4.11 (3H, s), 3.08 (2H, t, J = 6.8 Hz)

Mass spectrometry value (ESI-MS, m/z): 514 (M⁺+1)

Example 86: 3-(Trifluoromethyl)phenethyl N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0188] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (85 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (125 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-trifluoromethylphenethyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (69 mg, yield 46%).

¹H-NMR (CDCl₃, 400 MHz): 8.79 (1H, s), 8.27 - 8.34 (1H, m), 8.03 (1H, s), 7.30 - 7.62 (6H, m), 7.24 - 7.23 (2H, m), 4.46 (2H, t, J = 6.8 Hz), 4.18 (3H, s), 4.11 (3H, s), 3.10 (2H, t, J = 6.9 Hz)

Mass spectrometry value (ESI-MS, m/z): 549 (M⁺+1)

Example 87: 1-[3-(Trifluoromethyl)phenyl]ethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]carbamate

[0189] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (74 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (115 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-trifluoromethyl- α -methylbenzyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (81 mg, yield 59%).

¹H-NMR (CDCl₃, 400 MHz): 8.41 - 8.48 (1H, m), 8.11 (1H, s), 7.45 - 7.68 (7H, m), 7.13 - 7.18 (2H, m), 6.93 (1H, s), 6.65 (1H, d, J = 6.6 Hz), 5.94 (1H, q, J = 6.6 Hz), 4.14 (3H, s), 4.08 (3H, s), 1.63 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 513 (M⁺+1)

Example 88: 1-[3-(Trifluoromethyl)phenyl]ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0190] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (72 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (110 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-trifluoromethyl- α -methylbenzyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (90 mg, yield 68%).

¹H-NMR (CDCl₃, 400 MHz): 8.39 - 8.45 (1H, m), 8.13 (1H, s), 7.40 - 7.72 (6H, m), 6.99 (1H, d, J = 9.0 Hz), 6.48 - 6.55 (2H, m), 5.93 (1H, t, J = 6.6 Hz), 4.15 (3H, s), 4.09 (3H, s), 2.24 (3H, s), 2.07 (3H, s), 1.63 (3H, d, J = 6.6 Hz)
Mass spectrometry value (ESI-MS, m/z): 542 (M⁺+1)

Example 89: 1-[3-(Trifluoromethyl)phenyl]ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0191] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (76 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (110 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-trifluoromethyl- α -methylbenzyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (78 mg, yield 58%).

¹H-NMR (CDCl₃, 400 MHz): 8.40 - 8.47 (1H, m), 8.12 (1H, s), 7.84 (1H, s), 7.45 - 7.68 (5H, m), 6.93 (1H, s), 6.47 - 6.57 (2H, m), 5.93 (1H, q, J = 6.8 Hz), 4.14 (3H, s), 4.08 (3H, s), 2.27 (3H, s), 2.09 (3H, s), 1.63 (3H, d, J = 6.8 Hz)
Mass spectrometry value (ESI-MS, m/z): 542 (M⁺+1)

Example 90: 1-[3-(Trifluoromethyl)phenyl]ethyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0192] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (89 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-trifluoromethyl- α -methylbenzyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (80 mg, yield 48%).

¹H-NMR (CDCl₃, 400 MHz) : 8.75 (1H, s), 8.07 (1H, s), 7.14 - 7.63 (8H, m), 6.95 (1H, s), 6.79 (1H, d, J = 8.8 Hz), 5.93 (1H, q, J = 6.6 Hz), 4.15 (3H, s), 4.09 (3H, s), 1.61 (3H, d, J = 6.6 Hz)
Mass spectrometry value (ESI-MS, m/z): 514 (M⁺+1)

Example 91: 1-[3-(Trifluoromethyl)phenyl]ethyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0193] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (76 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-trifluoromethyl- α -methylbenzyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (53 mg, yield 39%).

¹H-NMR (CDCl₃, 400 MHz): 8.76 (1H, s), 7.86 (1H, s), 7.20 - 7.65 (6H, m), 6.88 - 6.92 (2H, m), 6.72 - 6.77 (1H, m), 5.87 - 5.95 (1H, m), 4.15 (3H, s), 4.09 (3H, s), 1.60 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 549 (M⁺+1)

Example 92: 1-(2,4,5-Trifluorophenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0194] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (87 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (130 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2,4,5-trifluoro- α -methylbenzyl alcohol (80 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (77 mg, yield 49%).

¹H-NMR (CDCl₃, 400 MHz): 8.41 - 8.49 (1H, m), 8.11 (1H, s), 7.56 - 7.64 (4H, m), 7.12 - 7.20 (2H, m), 6.80 - 6.72 (2H, m), 6.65 (1H, d, J = 6.4 Hz), 6.07 (1H, q, J = 6.4 Hz), 4.14 (3H, s), 4.08 (3H, s), 1.59 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 499 (M⁺+1)

Example 93: 1-(2,4,5-Trifluorophenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0195] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (76 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (130 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2,4,5-trifluoro- α -methylbenzyl alcohol (80 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (61 mg, yield 46%).

¹H-NMR (CDCl₃, 400 MHz): 8.40 - 8.47 (1H, m), 8.13 (1H, s), 7.62 - 7.74 (2H, m), 6.82 - 6.72 (3H, m), 6.48 - 6.55 (2H, m), 6.07 (1H, q, J = 6.6 Hz), 4.15 (3H, s), 4.09 (3H, s), 2.26 (3H, s), 2.08 (3H, s), 1.59 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 528 (M⁺+1)

Example 94: 1-(2,4,5-Trifluorophenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0196] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (82 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (130 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2,4,5-trifluoro- α -methylbenzyl alcohol (80 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (68 mg, yield 48%).

¹H-NMR (CDCl₃, 400 MHz): 8.4-8.48 (1H, m), 8.11 (1H, s), 7.84 (1H, s), 7.61 (1H, s), 6.80 - 7.30 (3H, m), 6.52 - 6.57 (2H, m), 6.06 (1H, q, J = 6.7 Hz), 4.14 (3H, s), 4.08 (3H, s), 2.28 (3H, s), 2.09 (3H, s), 1.59 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 527 (M⁺+1)

Example 95: 1-(2,4,5-Trifluorophenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0197] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (89 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (130 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2,4,5-trifluoro- α -methylbenzyl alcohol (80 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (51 mg, yield 32%).

¹H-NMR (CDCl₃, 400 MHz) : 8.73 (1H, s), 8.05 (1H, s), 7.58 (1H, s), 7.53 - 7.58 (1H, m), 6.50 - 7.25 (6H, m), 6.00 - 6.10 (1H, m), 4.15 (3H, s), 4.09 (3H, s), 1.57 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 500 (M⁺+1)

5 Example 96: 1-(2,4,5-Trifluorophenyl)ethyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}carbamate

[0198] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (130 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2,4,5-trifluoro- α -methylbenzyl alcohol (80 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (48 mg, yield 35%).

¹H-NMR (CDCl₃, 400 MHz): 8.72 (1H, s), 8.27 (1H, d, J = 9.0 Hz), 7.99 (1H, s), 7.50 (1H, s), 6.80 - 7.28 (5H, m), 5.95 - 6.08 (1H, m), 4.11 (3H, s), 4.04 (3H, s), 1.56 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 535 (M⁺+1)

20 Example 97: 1-(3-Fluorophenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0199] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (97 mg) was added to toluene/triethylamine = 10/1 (10 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (150 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-fluoro- α -methylbenzyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (111 mg, yield 68%).

¹H-NMR (CDCl₃, 400 MHz): 8.41 - 8.47 (1H, m), 8.12 (1H, s), 7.55 - 7.62 (3H, m), 6.86 - 7.38 (7H, m), 6.65 (1H, d, J = 6.6 Hz), 5.88 (1H, t, J = 6.6 Hz), 4.14 (3H, s), 4.08 (3H, s), 1.60 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 463 (M⁺+1)

35 Example 98: 1-(3-Fluorophenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0200] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (86 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (150 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-fluoro- α -methylbenzyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (89 mg, yield 64%).

¹H-NMR (CDCl₃, 400 MHz): 8.38 - 8.44 (1H, m), 8.13 (1H, s), 7.66 - 7.75 (1H, m), 7.64 (1H, s), 6.95 - 7.36 (6H, m), 6.51 (1H, d, J = 6.4 Hz), 5.87 (1H, q, J = 6.6 Hz), 4.15 (3H, s), 4.09 (3H, s), 2.25 (3H, s), 2.07 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

50 Example 99: 1-(3-Fluorophenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0201] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (97 mg) was added to toluene/triethylamine = 10/1 (10 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (150 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-fluoro- α -methylbenzyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate

and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (108 mg, yield 68%).

¹H-NMR (CDCl₃, 400 MHz): 8.40 - 8.45 (1H, m), 8.12 (1H, s), 7.87 (1H, s), 7.62 (1H, s), 6.90 - 7.38 (5H, m), 6.54 (1H, d, J = 6.8 Hz), 6.49 (1H, s), 4.15 (3H, s), 4.08 (3H, s), 2.27 (3H, s), 2.09 (3H, s), 1.61 (3H, d, J = 6.8 Hz)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

Example 100: 1-(3-Fluorophenyl)ethyl N-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0202] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (99 mg) was added to toluene/triethylamine = 10/1 (10 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (150 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-fluoro- α -methylbenzyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (60 mg, yield 36%).

¹H-NMR (CDCl₃, 400 MHz): 8.75 (1H, s), 7.98 (1H, bs), 8.47 (1H, bs), 6.48 - 7.60 (9H, m), 5.82 - 5.90 (1H, m), 4.13 (3H, s), 4.08 (3H, s), 1.58 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 464 (M⁺+1)

Example 101: 1-(3-Fluorophenyl)ethyl N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0203] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (98 mg) was added to toluene/triethylamine = 10/1 (10 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (150 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-fluoro- α -methylbenzyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (49 mg, yield 31%).

¹H-NMR (CDCl₃, 400 MHz): 8.78 (1H, s), 8.34 (1H, d, J = 9.3 Hz), 8.13 (1H, s), 7.56 (1H, s), 6.97 - 7.38 (7H, m), 5.88 (1H, q, J = 6.5 Hz), 4.17 (3H, s), 4.17 (3H, s), 4.10 (3H, s), 1.61 (3H, d, J = 6.8 Hz)

Mass spectrometry value (ESI-MS, m/z): 499 (M⁺+1)

Example 102: 1-(4-Fluorophenyl)ethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]carbamate

[0204] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-fluoro- α -methylbenzyl alcohol (57 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (91 mg, yield 73%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 - 8.48 (1H, m), 8.14 (1H, s), 7.63 (1H, s), 7.57 - 7.61 (2H, m), 7.37 - 7.42 (2H, m), 7.14 - 7.19 (2H, m), 7.04 - 7.10 (2H, m), 6.86 (1H, s), 6.66 (1H, d, J = 6.6 Hz), 5.90 (1H, q, J = 6.6 Hz), 4.16 (3H, s), 4.10 (3H, s), 1.62 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 461 (M⁺+1)

Example 103: 1-(4-Fluorophenyl)ethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0205] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (86 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (117 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-fluoro- α -methylbenzyl alcohol (55 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2

hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (94 mg, yield 72%).

¹H-NMR (CDCl₃, 400 MHz): 8.42 - 8.48 (1H, m), 8.15 (1H, s), 7.74 (1H, d, J = 8.5 Hz), 7.66 (1H, s), 7.37 - 7.43 (2H, m), 6.98 - 7.10 (3H, m), 6.48 - 6.55 (2H, m), 5.90 (1H, q, J = 6.6 Hz), 4.17 (3H, s), 4.10 (3H, s), 2.25 (3H, s), 2.09 (3H, s), 1.63 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

Example 104: 1-(4-Fluorophenyl)ethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0206] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (90 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (123 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-fluoro- α -methylbenzyl alcohol (58 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (87 mg, yield 64%).

¹H-NMR (CDCl₃, 400 MHz): 8.40 - 8.48 (1H, m), 8.12 (1H, s), 7.88 (1H, s), 7.61 (1H, s), 7.30 - 7.41 (2H, m), 7.30 - 7.41 (2H, m), 7.00 - 7.10 (2H, m), 6.91 (1H, s), 6.53 (1H, d, J = 6.6 Hz), 6.45 (1H, s), 5.87 (1H, q, J = 6.7 Hz), 4.14 (3H, s), 4.08 (3H, s), 2.25 (3H, s), 2.09 (3H, s), 1.61 (3H, d, J = 6.7 Hz)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

Example 105: 1-(4-Fluorophenyl)ethyl N-[4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0207] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-fluoro- α -methylbenzyl alcohol (57 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (59 mg, yield 47%).

¹H-NMR (CDCl₃, 400 MHz) : 8.77 (1H, s), 8.08 (1H, s), 7.60 (1H, s), 7.52 - 7.58 (2H, m), 7.36 - 7.41 (2H, m), 7.16 - 7.20 (2H, m), 7.02 - 7.09 (2H, m), 6.79 (1H, s), 5.89 (1H, q, J = 6.6 Hz), 4.18 (3H, s), 4.11 (3H, s), 1.61 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 464 (M⁺+1)

Example 106: 1-(4-Fluorophenyl)ethyl N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0208] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (85 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (114 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-fluoro- α -methylbenzyl alcohol (54 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (45 mg, yield 35%).

¹H-NMR (CDCl₃, 400 MHz): 8.80 (1H, s), 8.35 (1H, d, J = 9.0 Hz), 8.12 (1H, s), 7.57 (1H, s), 7.05 - 7.44 (7H, m), 5.90 (1H, q, J = 6.6 Hz), 4.19 (3H, s), 4.11 (3H, s), 1.63 (3H, d, J = 6.8 Hz)

Mass spectrometry value (ESI-MS, m/z): 499 (M⁺+1)

Example 107: 4-Methylbenzyl {4-[(6,7-dimethoxy-4-quinolyl)oxy]anilino}methanethioate

[0209] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (82 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methylbenzylmercaptan (60 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (90 mg, yield 65%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 - 8.50 (1H, m), 8.13 (1H, s), 7.55 - 7.72 (4H, m), 7.00 - 7.26 (6H, m), 6.67 (1H, d, J = 6.4 Hz), 4.21 (2H, s), 4.16 (3H, s), 4.10 (3H, s), 2.33 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 462 (M⁺+1)

Example 108: 4-Methylbenzyl {4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylanilino}methanethioate

[0210] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (90 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (145 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methylbenzylmercaptan (60 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (87 mg, yield 60%).

¹H-NMR (CDCl₃, 400 MHz): 8.47 (1H, bs), 8.16 (1H, s), 7.58 - 7.70 (2H, m), 6.88 - 7.26 (6H, m), 6.6 (1H, bs), 4.21 (2H, s), 4.17 (3H, s), 4.11 (3H, s), 2.34 (3H, s), 2.27 (3H, s), 2.14 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 490 (M⁺+1)

Example 109: 4-Methylbenzyl {4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylanilino}methanethioate

[0211] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (90 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (145 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methylbenzylmercaptan (60 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (74 mg, yield 54%).

¹H-NMR (CDCl₃, 400 MHz): 8.45 - 8.52 (1H, m), 8.15 (1H, s), 7.80 (1H, s), 7.64 (1H, s), 6.89 - 7.28 (6H, m), 6.57 (1H, d, J = 6.3 Hz), 4.22 (2H, s), 4.17 (3H, s), 4.11 (3H, s), 2.34 (3H, s), 2.28 (3H, s), 2.13 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 490 (M⁺+1)

Example 110: 4-Methylbenzyl {4-[(6,7-dimethoxy-4-quinazolinyloxy]anilino}methanethioate

[0212] 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (81 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methylbenzylmercaptan (60 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (74 mg, yield 54%).

¹H-NMR (CDCl₃, 400 MHz): 8.72 (1H, s), 8.12 (1H, s), 7.50 - 7.67 (4H, m), 7.10 - 7.26 (6H, m), 4.21 (2H, s), 4.18 (3H, s), 4.12 (3H, s), 2.33 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 462 (M⁺+1)

Example 111: 4-Methylbenzyl {2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)anilino]methanethioate

[0213] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (85 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methylbenzylmercaptan (60 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (58 mg, yield 42%).

¹H-NMR (CDCl₃, 400 MHz): 8.81 (1H, s), 8.44 (1H, d, J = 9.3 Hz), 8.13 (1H, s), 7.52 - 7.55 (2H, m), 7.11 - 7.34 (6H, m), 4.24 (2H, s), 4.19 (3H, s), 4.12 (3H, s), 2.34 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 497 (M⁺+1)

Example 112: 1-(2-Bromophenyl)ethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]carbamate

[0214] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (88 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (145 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-bromo- α -methylbenzyl alcohol (90 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (89 mg, yield 54%).

¹H-NMR (CDCl₃, 400 MHz): 8.44 (1H, d, J = 6.7 Hz), 8.12 (1H, s), 6.90 - 7.61 (10H, m), 6.65 (1H, d, J = 6.7 Hz), 6.20 (1H, q, J = 6.4 Hz), 4.14 (3H, s), 4.08 (3H, s), 1.59 (3H, d, J = 6.4 Hz)

Mass spectrometry value (ESI-MS, m/z): 524 (M⁺+1)

Example 113: 1-(2-Bromophenyl)ethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0215] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (78 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (145 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-bromo- α -methylbenzyl alcohol (90 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (101 mg, yield 71%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 (1H, dd, J = 6.5 Hz), 8.15 (1H, s), 7.15 - 7.78 (6H, m), 7.00 (1H, d, J = 8.8 Hz), 6.57 (1H, bs), 6.52 (1H, d, J = 6.5 Hz), 6.21 (1H, q, J = 6.5 Hz), 4.17 (3H, s), 4.11 (3H, s), 2.28 (3H, s), 2.09 (3H, s), 1.62 (3H, d, J = 6.5 Hz)

Mass spectrometry value (ESI-MS, m/z): 552 (M⁺+1)

Example 114: 1-(2-Bromophenyl)ethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0216] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (85 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (148 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-bromo- α -methylbenzyl alcohol (90 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (70 mg, yield 45%).

¹H-NMR (CDCl₃, 400 MHz): 8.45 (1H, dd, J = 6.6 Hz), 8.14 (1H, s), 7.92 (1H, bs), 7.15 - 7.65 (6H, m), 6.94 (1H,

s), 6.46 - 6.58 (2H, m), 6.22 (1H, q, J = 6.6 Hz), 4.17 (3H, s), 4.10 (3H, s), 2.30 (3H, s), 2.10 (3H, s), 1.63 (3H, d, J = 6.6 Hz)
Mass spectrometry value (ESI-MS, m/z): 552 (M⁺+1)

Example 115: 1-(2-Bromophenyl)ethyl N-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0217] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (90 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-bromo- α -methylbenzyl alcohol (90 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (60 mg, yield 35%).

¹H-NMR (CDCl₃, 400 MHz): 8.75 (1H, s), 8.04 (1H, s), 7.14 - 7.61 (9H, m), 6.94 (1H, bs), 6.20 (1H, q, J = 6.5 Hz), 4.17 (3H, s), 4.11 (3H, s), 1.60 (3H, d, J = 6.5 Hz)

Mass spectrometry value (ESI-MS, m/z): 525 (M⁺+1)

Example 116: 1-(2-Bromophenyl)ethyl N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0218] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (85 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (139 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-bromo- α -methylbenzyl alcohol (90 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (51 mg, yield 33%).

¹H-NMR (CDCl₃, 400 MHz): 8.80 (1H, s), 8.38 (1H, d, J = 9.3 Hz), 8.14 (1H, s), 7.16 - 7.60 (7H, m), 6.23 (1H, q, J = 6.6 Hz), 4.19 (3H, s), 4.11 (3H, s), 1.63 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 560 (M⁺+1)

Example 117: 1-(3-Bromophenyl)ethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]carbamate

[0219] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (72 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (111 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-bromo- α -methylbenzyl alcohol (75 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (79 mg, yield 584%).

¹H-NMR (CDCl₃, 400 MHz): 8.46 (1H, dd, J = 6.4 Hz), 8.13 (1H, s), 7.16 - 7.64 (9H, m), 7.01 (1H, s), 6.68 (1H, d, J = 6.4 Hz), 5.86 (1H, q, J = 6.4 Hz), 4.16 (3H, s), 4.10 (3H, s), 1.61 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 524 (M⁺+1)

Example 118: 1-(3-Bromophenyl)ethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0220] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (68 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-bromo- α -methylbenzyl alcohol (75 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound

(83 mg, yield 67%).

¹H-NMR (CDCl₃, 400 MHz): 8.45 (1H, dd, J = 6.6 Hz), 8.15 (1H, s like), 7.16 - 7.74 (7H, m), 7.02 (1H, d, J = 9.0 Hz), 6.54 (1H, d, J = 6.1 Hz), 5.86 (1H, q, J = 6.6 Hz), 4.17 (3H, s), 4.11 (3H, s), 2.27 (3H, s), 2.10 (3H, s), 1.62 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 552 (M⁺+1)

Example 119: 1-(3-Bromophenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0221] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (88 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (138 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-bromo- α -methylbenzyl alcohol (75 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (88 mg, yield 55%).

¹H-NMR (CDCl₃, 400 MHz): 8.40 - 8.50 (1H, m), 8.15 (1H, s like), 7.89 (1H, bs), 7.20 - 7.66 (5H, m), 6.95 (1H, s), 6.56 (1H, d, J = 6.4 Hz), 6.50 (1H, bs), 5.86 (1H, q, J = 6.6 Hz), 4.17 (3H, s), 4.10 (3H, s), 2.30 (3H, s), 2.11 (3H, s), 1.62 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 552 (M⁺+1)

Example 120: 1-(3-Bromophenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}carbamate

[0222] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (74 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (125 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-bromo- α -methylbenzyl alcohol (75 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (61 mg, yield 44%).

¹H-NMR (CDCl₃, 400 MHz): 8.76 (1H, s), 8.06 (1H, s), 7.16 - 7.62 (8H, m), 6.85 (1H, bs), 5.85 (1H, q, J = 6.6 Hz), 4.18 (3H, s), 4.11 (3H, s), 1.65 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 525 (M⁺+1)

Example 121: 1-(3-Bromophenyl)ethyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}carbamate

[0223] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (76 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (119 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-bromo- α -methylbenzyl alcohol (75 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (51 mg, yield 40%).

¹H-NMR (CDCl₃, 400 MHz): 8.80 (1H, s), 8.35 (1H, d, J = 9.0 Hz), 8.12 (1H, s), 7.54 - 7.60 (2H, m), 7.44 - 7.58 (1H, m), 7.15 - 7.36 (4H, m), 5.86 (1H, q, J = 6.7 Hz), 4.19 (3H, s), 4.16 (3H, s), 1.63 (3H, d, J = 6.7 Hz)

Mass spectrometry value (ESI-MS, m/z): 560 (M⁺+1)

Example 122: 1-(2-Fluorophenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0224] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (77 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (117 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-fluoro- α -methylbenzyl alcohol (55 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the

completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (101 mg, yield 78%).

Mass spectrometry value (ESI-MS, m/z): 524 (M⁺+1)

Example 123: 1-(2-Fluorophenyl)ethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0225] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (74 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (103 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-fluoro- α -methylbenzyl alcohol (55 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (88 mg, yield 73%).

¹H-NMR (CDCl₃, 400 MHz): 8.37 (1H, dd, J = 6.6 Hz), 8.08 (1H, s like), 7.67 (1H, d, J = 8.1 Hz), 7.59 (1H, s), 7.37 (1H, dd, J = 7.1 Hz), 7.10 (1H, dd, J = 7.4 Hz), 7.01 (1H, dd, J = 9.4 Hz), 6.93 (1H, d, J = 8.8 Hz), 6.50 (1H, s), 6.46 (1H, d, J = 6.6 Hz), 6.10 (1H, q, J = 6.6 Hz), 4.10 (3H, s), 4.04 (3H, s), 2.22 (3H, s), 2.02 (3H, s), 1.59 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

Example 124: 1-(2-Fluorophenyl)ethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0226] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (71 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (99 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-fluoro- α -methylbenzyl alcohol (55 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (78 mg, yield 68%).

¹H-NMR (CDCl₃, 400 MHz): 8.45 (1H, dd, J = 6.5 Hz), 8.15 (1H, d, J = 4.2 Hz), 7.91 (1H, s), 7.64 (1H, s), 7.42 - 7.45 (1H, m), 7.28 - 7.33 (1H, m), 7.06 - 7.11 (1H, m), 7.15 - 7.20 (1H, m), 6.94 (1H, s), 6.56 (1H, d, J = 6.5 Hz), 6.52 (1H, s), 6.17 (1H, q, J = 6.7 Hz), 4.17 (3H, s), 4.10 (3H, s), 2.29 (3H, s), 2.11 (3H, s), 1.66 (3H, d, J = 6.7 Hz)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

Example 125: 1-(2-Fluorophenyl)ethyl N-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0227] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (90 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (136 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-fluoro- α -methylbenzyl alcohol (55 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (79 mg, yield 52%).

¹H-NMR (CDCl₃, 400 MHz): 8.74 (1H, s), 8.06 (1H, s), 7.58 (1H, s), 7.54 (2H, d, J = 9.0 Hz), 7.39 - 7.43 (1H, m), 7.23 - 7.32 (1H, m), 7.12 - 7.17 (3H, m), 7.03 - 7.08 (1H, m), 6.86 (1H, s), 6.14 (1H, q, J = 6.6 Hz), 4.15 (3H, s), 4.09 (3H, s), 1.62 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 464 (M⁺+1)

Example 126: 1-(2-Fluorophenyl)ethyl N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0228] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (83 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (134 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-fluoro- α -methylbenzyl alcohol (55 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (60 mg, yield 45%).

¹H-NMR (CDCl₃, 400 MHz): 8.80 (1H, s), 8.37 (1H, d, J = 9.2 Hz), 8.15 (1H, s), 7.58 (1H, s), 7.43 - 7.52 (1H, m), 7.32 (1H, d, J = 2.7 Hz), 7.28 - 7.35 (1H, m), 7.15 - 7.20 (2H, m), 7.06 - 7.11 (1H, m), 6.19 (1H, q, J = 6.6 Hz), 4.19 (3H, s), 4.12 (3H, s), 1.66 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 499 (M⁺+1)

Example 127: 1-(2-Ethoxyphenyl)ethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]carbamate

[0229] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (122 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-ethoxy- α -methylbenzyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (98 mg, yield 69%).

¹H-NMR (CDCl₃, 400 MHz): 8.46 (1H, dd, J = 6.5 Hz), 8.14 (1H, s like), 7.58 - 7.64 (3H, m), 7.38 - 7.42 (1H, m), 7.16 - 7.18 (2H, m), 6.85 - 7.00 (3H, m), 6.68 (1H, d, J = 6.6 Hz), 6.31 (1H, q, J = 6.5 Hz), 4.16 (3H, s), 4.10 (3H, s), 4.05 - 4.13 (2H, m), 1.59 (3H, d, J = 6.5 Hz), 1.44 (3H, t, J = 7.1 Hz)

Mass spectrometry value (ESI-MS, m/z) : 490 (M⁺+1)

Example 128: 1-(2-Ethoxyphenyl)ethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0230] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (72 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (100 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-ethoxy- α -methylbenzyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (71 mg, yield 58%).

¹H-NMR (CDCl₃, 400 MHz): 8.42 (1H, d, J = 6.5 Hz), 8.13 (1H, s like), 7.73 - 7.80 (1H, m), 7.64 (1H, s), 7.10 - 7.40 (2H, m), 6.80 - 7.00 (3H, m), 6.48 - 6.53 (1H, m), 6.28 (1H, q, J = 6.4 Hz), 4.15 (3H, s), 4.09 (3H, s), 4.02 - 4.10 (2H, m), 2.24 (3H, s), 2.07 (3H, s), 1.57 (3H, d, J = 6.4 Hz), 1.42 (3H, t, J = 6.9 Hz)

Mass spectrometry value (ESI-MS, m/z): 518 (M⁺+1)

Example 129: 1-(2-Ethoxyphenyl)ethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0231] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (83 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (115 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-ethoxy- α -methylbenzyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound

(78 mg, yield 55%).

¹H-NMR (CDCl₃, 400 MHz): 8.42 (1H, dd, J = 6.3 Hz), 8.13 (1H, s like), 7.93 (1H, bs), 7.38 (1H, d, J = 7.6 Hz), 6.83 - 6.99 (4H, m), 6.53 - 6.58 (1H, m), 6.49 (1H, bs), 6.19 (1H, q, J = 6.5 Hz), 4.15 (3H, s), 4.08 (3H, s), 4.04 - 4.11 (2H, m), 2.27 (3H, s), 2.08 (3H, s), 1.58 (3H, d, J = 6.5 Hz), 1.43 (3H, t, J = 6.9 Hz)

Mass spectrometry value (ESI-MS, m/z) : 518 (M⁺+1)

Example 130: 1-(2-Ethoxyphenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0232] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (77 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (117 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-ethoxy- α -methylbenzyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (63 mg, yield 46%).

¹H-NMR (CDCl₃, 400 MHz): 8.74 (1H, s like), 8.05 (1H, s), 7.53 - 7.59 (3H, m), 7.34 - 7.38 (1H, m), 7.13 - 7.26 (3H, m), 6.82 - 6.98 (3H, m), 6.27 (1H, q, J = 6.5 Hz), 4.15 (3H, s), 4.09 (3H, s), 4.02 - 4.10 (2H, m), 1.56 (3H, d, J = 6.5 Hz), 1.42 (3H, t, J = 7.0 Hz)

Mass spectrometry value (ESI-MS, m/z): 491 (M⁺+1)

Example 131: 1-(2-Ethoxyphenyl)ethyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0233] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (80 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (109 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-ethoxy- α -methylbenzyl alcohol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (58 mg, yield 43%).

¹H-NMR (CDCl₃, 400 MHz) : 8.80 (1H, s), 8.40 (1H, d, J = 9.0 Hz), 8.13 (1H, s), 7.58 (1H, s), 7.14 - 7.45 (4H, m), 6.86 - 7.01 (3H, m), 6.32 (1H, q, J = 6.3 Hz), 4.19 (3H, s), 4.12 (3H, s), 4.05 - 4.13 (2H, m), 1.61 (3H, d, J = 6.3 Hz), -1.39 - 1.45 (3H, m)

Mass spectrometry value (ESI-MS, m/z): 525 (M⁺+1)

Example 132: 1-(4-Methylphenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0234] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (72 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (109 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methyl- α -methylbenzyl alcohol (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (98 mg, yield 81%).

¹H-NMR (CDCl₃, 400 MHz): 8.40 - 8.45 (1H, m), 8.11 (1H, s), 7.61 (1H, s), 7.53 - 7.59 (2H, m), 7.10 - 7.32 (6H, m), 6.78 - 6.85 (1H, m), 6.65 (1H, d, J = 6.6 Hz), 5.87 (1H, q, J = 6.6 Hz), 4.14 (3H, s), 4.08 (3H, s), 2.34 (3H, s), 1.60 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 460 (M⁺+1)

Example 133: 1-(4-Methylphenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0235] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (111 mg) in methylene

chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methyl- α -methylbenzyl alcohol (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (97 mg, yield 75%).

$^1\text{H-NMR}$ (CDCl_3 , 400 MHz): 8.40 - 8.45 (1H, m), 8.12 (1H, s), 7.73 (1H, d, $J = 8.3$ Hz), 7.64 (1H, s), 7.15 - 7.32 (4H, m), 6.97 (1H, d, $J = 8.8$ Hz), 6.51 (1H, d, $J = 6.6$ Hz), 6.48 (1H, s), 5.87 (1H, q, $J = 6.5$ Hz), 4.14 (3H, s), 4.08 (3H, s), 2.34 (3H, s), 2.22 (3H, s), 2.06 (3H, s), 1.60 (3H, d, $J = 6.4$ Hz)

Mass spectrometry value (ESI-MS, m/z): 488 ($M^+ + 1$)

Example 134: 1-(4-Methylphenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0236] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (111 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methyl- α -methylbenzyl alcohol (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (88 mg, yield 68%).

$^1\text{H-NMR}$ (CDCl_3 , 400 MHz): 8.41 - 8.47 (1H, m), 8.12 (1H, s), 7.90 (1H, s), 7.62 (1H, s), 7.15 - 7.33 (4H, m), 6.91 (1H, s), 6.54 (1H, d, $J = 6.4$ Hz), 6.45 (1H, s), 5.87 (1H, q, $J = 6.6$ Hz), 4.14 (3H, s), 4.08 (3H, s), 2.34 (3H, s), 2.22 (3H, s), 2.08 (3H, s), 1.61 (3H, d, $J = 6.6$ Hz)

Mass spectrometry value (ESI-MS, m/z): 488 ($M^+ + 1$)

Example 135: 1-(4-Methylphenyl)ethyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0237] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (76 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (115 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methyl- α -methylbenzyl alcohol (52 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (85 mg, yield 67%).

$^1\text{H-NMR}$ (CDCl_3 , 400 MHz): 8.74 (1H, s), 8.03 (1H, s), 7.43 - 7.60 (3H, m), 6.74 - 7.30 (6H, m), 6.45 (1H, bs), 5.80 - 5.90 (1H, m), 4.14 (3H, s), 4.09 (3H, s), 2.33 (3H, s), 1.59 (3H, d, $J = 6.6$ Hz)

Mass spectrometry value (ESI-MS, m/z): 461 ($M^+ + 1$)

Example 136: 1-(4-Methylphenyl)ethyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0238] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (78 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (106 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-methyl- α -methylbenzyl alcohol (48 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (61 mg, yield 49%).

$^1\text{H-NMR}$ (CDCl_3 , 400 MHz): 8.78 (1H, s), 8.35 (1H, d, $J = 9.0$ Hz), 8.12 (1H, s), 7.55 (1H, s), 7.12 - 7.34 (7H, m), 5.83 - 5.91 (1H, m), 4.17 (3H, s), 4.09 (3H, s), 2.34 (3H, s), 1.62 (3H, d, $J = 6.5$ Hz)

Mass spectrometry value (ESI-MS, m/z): 405 ($M^+ + 1$)

Example 137: 3-[(4-Methylphenyl)sulfanyl]ethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-phenyl]carbamate

[0239] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (78 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (118 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-[(4-methylphenyl)sulfanyl]-1-ethanol (66 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (48 mg, yield 35%).

¹H-NMR (CDCl₃, 400 MHz): 8.40 - 8.49 (1H, M), 8.13 (1H, s), 7.62 (1H, s), 7.55 (1H, d, J = 9.0 Hz), 7.09 - 7.35 (6H, m), 6.75 (1H, s), 6.66 (1H, d, J = 6.4 Hz), 4.33 (2H, t, J = 6.4 Hz), 4.15 (3H, s), 4.08 (3H, s), 3.15 (2H, t, J = 6.4 Hz), 2.31 (3H, s)

Mass spectrometry value (ESI-MS, m/z) : 492 (M⁺+1)

Example 138: 3-[(4-Methylphenyl)sulfanyl]ethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0240] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (72 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (100 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-[(4-methylphenyl)sulfanyl]-1-ethanol (56 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (53 mg, yield 43%).

¹H-NMR (CDCl₃, 400 MHz) : 8.40 - 8.46 (1H, m), 8.13 (1H, s), 7.63 - 7.74 (2H, m), 6.98 - 7.36 (5H, m), 5.53 (1H, d, J = 6.6 Hz), 6.43 (1H, s), 4.33 (2H, t, J = 6.7 Hz), 4.15 (3H, s), 4.09 (3H, s), 3.16 (2H, t, J = 6.7 Hz), 2.30 (6H, s), 2.23 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 520 (M⁺+1)

Example 139: 3-[(4-Methylphenyl)sulfanyl]ethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0241] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (74 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (103 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-[(4-methylphenyl)sulfanyl]-1-ethanol (58 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (51 mg, yield 40%).

¹H-NMR (CDCl₃, 400 MHz): 8.41 - 8.48 (1H, m), 8.13 (1H, s), 7.85 (1H, s), 7.62 (1H, s), 6.92 - 7.35 (5H, m), 6.55 (1H, d, J = 6.1 Hz), 6.39 (1H, s), 4.33 (1H, t, J = 6.7 Hz), 4.15 (3H, s), 4.08 (3H, s), 3.16 (2H, t, J = 6.7 Hz), 2.31 (3H, s), 2.24 (3H, s), 2.14 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 520 (M⁺+1)

Example 140: 3-[(4-Methylphenyl)sulfanyl]ethyl N-[4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0242] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (69 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (105 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-[(4-methylphenyl)sulfanyl]-1-ethanol (59 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound

(29 mg, yield 24%).

¹H-NMR (CDCl₃, 400 MHz): 8.76 (1H, s), 8.10 (1H, s), 7.59 (1H, s), 7.49 - 7.56 (2H, m), 6.70 - 7.33 (7H, m), 4.32 (2H, t, J = 6.7 Hz), 4.17 (3H, s), 4.10 (3H, s), 3.14 (2H, t, J = 6.7 Hz), 2.31 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 493 (M⁺+1)

Example 141: 3-[(4-Methylphenyl)sulfanyl]ethyl N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0243] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (75 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (102 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-[(4-methylphenyl)sulfanyl]-1-ethanol (57 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (57 mg, yield 30%).

¹H-NMR (CDCl₃, 400 MHz): 8.79 (1H, s), 8.32 (1H, d, J = 9.3 Hz), 8.13 (1H, s), 7.56 (1H, s), 7.08 - 7.36 (7H, m), 4.35 (2H, t, J = 6.7 Hz), 4.18 (3H, s), 4.10 (3H, s), 3.16 (2H, t, J = 6.7 Hz), 2.30 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 527 (M⁺+1)

Example 142: 3-(2-Fluorophenoxy)propyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]carbamate

[0244] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (70 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (106 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(2-fluorophenoxy)-1-propanol (60 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (60 mg, yield 55%).

¹H-NMR (CDCl₃, 400 MHz): 8.44 - 8.47 (1H, m), 8.11 - 8.13 (1H, m), 7.54 - 7.60 (2H, m), 7.61 (1H, s), 7.14 - 7.18 (2H, m), 7.01 - 7.08 (2H, m), 6.86 - 6.98 (3H, m), 4.14 (3H, s), 4.08 (3H, s), 4.11 - 4.20 (2H, m), 4.34 - 4.44 (2H, m), 2.12 - 2.24 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 494 (M⁺+1)

Example 143: 3-(2-Fluorophenoxy)propyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0245] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (72 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (100 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(2-fluorophenoxy)-1-propanol (57 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (78 mg, yield 63%).

¹H-NMR (CDCl₃, 400 MHz): 8.41 - 8.46 (1H, m), 8.13 - 8.14 (1H, d, J = 3.9 Hz), 7.72 (1H, s like), 7.64 (1H, s), 5.94 - 7.09 (3H, m), 6.87 - 6.93 (1H, m), 6.53 (1H, d, J = 6.6 Hz), 6.47 (1H, s), 4.42 (1H, t, J = 6.2 Hz), 4.35 (1H, t, J = 6.2 Hz), 4.15 - 4.20 (2H, m), 4.15 (3H, s), 4.09 (3H, s), 2.25 (3H, s), 2.08 (3H, s), 2.14 - 2.25 (2H, m)

Mass spectrometry value (ESI-MS, m/z) : 522 (M⁺+1)

Example 144: 3-(2-Fluorophenoxy)propyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0246] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (71 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (100 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(2-fluorophenoxy)-1-propanol (61 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2

hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (53 mg, yield 42%).

¹H-NMR (CDCl₃, 400 MHz): 8.45 - 8.49 (1H, m), 8.13 (1H, d like), 7.87 (1H, s), 7.62 (1H, s), 6.87 - 7.09 (4H, m), 6.56 (1H, d, J = 6.3 Hz), 6.45 (1H, s), 4.42 (1H, d, J = 6.2 Hz), 4.36 (1H, d, J = 6.2 Hz), 4.13 - 4.20 (2H, m), 4.15 (3H, s), 4.08 (3H, s), 2.05 - 2.24 (2H, m), 2.26 (3H, s), 2.10 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 522 (M⁺+1)

Example 145: 3-(2-Fluorophenoxy)propyl N-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0247] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (65 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (90 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(2-fluorophenoxy)-1-propanol (51 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (52 mg, yield 46%).

¹H-NMR (CDCl₃, 400 MHz): 8.74 (1H, s), 7.96 (1H, s), 7.58 (1H, s), 7.52 - 7.56 (1H, m), 7.16 - 7.21 (2H, m), 6.77 - 7.08 (5H, m), 4.40 (1H, t, J = 6.2 Hz), 4.34 (1H, t, J = 6.2 Hz), 4.07 - 4.19 (2H, m), 4.14 (3H, s), 4.09 (3H, s), 2.03 - 2.27 (2H, m)

Mass spectrometry value (ESI-MS, m/z) : 494 (M⁺+1)

Example 146: 3-(2-Fluorophenoxy)propyl N-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2,3-dimethylphenyl]carbamate

[0248] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2,3-dimethylaniline (65 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (90 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(2-fluorophenoxy)-1-propanol (51 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (52 mg, yield 46%).

¹H-NMR (CDCl₃, 400 MHz): 8.69 (1H, s like), 8.07 (1H, s), 7.65 (1H, bs), 7.57 (1H, s), 6.80 - 6.87 (1H, m), 6.89 - 7.04 (4H, m), 4.35 (1H, t, J = 6.2 Hz), 4.28 (1H, d, J = 6.2 Hz), 4.08 - 4.14 (2H, m), 4.12 (3H, s), 4.06 (3H, s), 2.05 - 2.19 (2H, m), 2.00 (3H, s)

Mass spectrometry value (ESI-MS, m/z) : 523 (M⁺+1)

Example 147: 3-(3-Fluorophenoxy)propyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]carbamate

[0249] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (71 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (108 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(3-fluorophenoxy)-1-propanol (61 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (88 mg, yield 69%).

¹H-NMR (CDCl₃, 400 MHz): 8.44 - 8.48 (1H, m), 8.12 (1H, d, J = 3.7 Hz), 7.61 (1H, s), 7.57 - 7.61 (2H, m), 7.14 - 7.21 (3H, m), 6.92 (1H, d, J = 9.2 Hz), 6.57 - 6.68 (3H, m), 4.39 (1H, t, J = 6.2 Hz), 4.35 (1H, d, J = 6.2 Hz), 4.12 (3H, s), 4.08 (3H, s), 4.05 - 4.09 (2H, m), 2.12 - 2.1 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 494 (M⁺+1)

Example 148: 3-(3-Fluorophenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0250] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (66 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (92 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(3-fluorophenoxy)-1-propanol (52 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (63 mg, yield 55%).

¹H-NMR (CDCl₃, 400 MHz): 8.41 - 8.45 (1H, m), 8.14 (1H, d, J = 3.9 Hz), 7.72 (1H, bs), 7.64 (1H, s), 7.16 - 7.22 (1H, m), 7.00 (1H, dd, J = 8.8 Hz, J = 5.6 Hz), 6.58 - 6.70 (2H, m), 6.53 (1H, d, J = 6.6 Hz), 6.43 - 6.49 (1H, m), 4.39 (1H, t, J = 6.2 Hz), 4.35 (1H, t, J = 6.2 Hz), 4.15 (3H, s), 4.10 (3H, s), 4.05 - 4.10 (2H, m), 2.25 (3H, d, J = 4.9 Hz), 2.08 (3H, s, J = 3.2 Hz), 2.13 - 2.21 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 522 (M⁺+1)

Example 149: 3-(3-Fluorophenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0251] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (79 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (110 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(3-fluorophenoxy)-1-propanol (62 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (74 mg, yield 54%).

¹H-NMR (CDCl₃, 400 MHz): 8.45 - 8.50 (1H, m), 8.12 (1H, d, J = 3.7 Hz), 7.86 (1H, bs), 7.62 (1H, s), 7.16 - 7.25 (1H, m), 6.93 (1H, d, J = 3.2 Hz), 6.54 - 6.70 (3H, m), 6.43 - 6.47 (1H, m), 4.39 (1H, t, J = 6.2 Hz), 4.36 (1H, t, J = 6.2 Hz), 4.14 (3H, s), 4.08 (3H, s), 4.05 - 4.10 (2H, m), 2.26 (3H, d, J = 4.6 Hz), 2.10 (3H, d, J = 5.4 Hz), 2.13 - 2.22 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 522 (M⁺+1)

Example 150: 3-(3-Fluorophenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0252] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (82 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (124 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(3-fluorophenoxy)-1-propanol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (59 mg, yield 46%).

¹H-NMR (CDCl₃, 400MHz): 8.69 (1H, s), 8.01 (1H, s), 7.54 (1H, s), 7.46 - 7.54 (2H, m), 7.10 - 7.15 (3H, m), 6.76 - 6.85 (1H, m), 6.51 - 6.64 (2H, m), 4.32 (1H, t, J = 6.2 Hz), 4.29 (1H, t, J = 6.2 Hz), 4.10 (3H, s), 4.04 (3H, s), 3.96 - 4.04 (2H, m), 2.05 - 2.15 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 494 (M⁺+1)

Example 151: 3-(3-Fluorophenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)-2,3-dimethylphenyl]carbamate

[0253] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2,3-dimethylaniline (68 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (94 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(3-fluorophenoxy)-1-propanol (53 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate

and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (68 mg, yield 56%).

¹H-NMR (CDCl₃, 400 MHz): 8.74 (1H, s), 8.08 (1H, s), 7.67 (1H, bs), 7.61 (1H, s), 7.14 - 7.23 (1H, m), 6.96 - 7.02 (1H, m), 6.55 - 6.68 (2H, m), 6.43 - 6.53 (1H, m), 4.30 - 4.38 (2H, m), 4.16 (3H, s), 4.10 (3H, s), 4.03 - 4.10 (2H, m), 2.22 - 2.25 (3H, m), 2.10 - 2.18 (2H, m), 2.04 - 2.07 (3H, m)

Mass spectrometry value (ESI-MS, m/z): 523 (M⁺+1)

Example 152: 3-(4-Fluorophenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0254] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (71 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (108 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(4-fluorophenoxy)-1-propanol (61 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (81 mg, yield 64%).

¹H-NMR (CDCl₃, 400 MHz): 8.45 (1H, d, J = 4.2 Hz), 8.12 (1H, d, J = 3.6 Hz), 7.62 (1H, s), 7.56 - 7.62 (2H, m), 7.14 - 7.18 (2H, m), 6.94 - 6.98 (1H, m), 6.80 - 6.89 (2H, m), 6.67 (1H, d, J = 6.4 Hz), 4.39 (1H, t, J = 6.2 Hz), 4.36 (1H, t, J = 6.2 Hz), 4.14 (3H, s), 4.08 (3H, s), 4.04 (2H, t, J = 6.0 Hz), 2.12 - 2.20 (2H, m)

Mass spectrometry value (ESI-MS, m/z) : 494 (M⁺+1)

Example 153: 3-(4-Fluorophenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0255] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (66 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (92 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(4-fluorophenoxy)-1-propanol (52 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (79 mg, yield 70%).

¹H-NMR (CDCl₃, 400 MHz): 8.44 (1H, dd, J = 6.2 Hz), 8.13 (1H, d, J = 3.9 Hz), 7.72 (1H, bs), 7.64 (1H, s), 6.92 - 7.02 (3H, m), 6.81 - 6.85 (1H, m), 6.53 (1H, d, J = 6.2 Hz), 6.48 (1H, d, J = 5.6 Hz), 4.39 (1H, t, J = 6.3 Hz), 4.35 (1H, t, J = 6.3 Hz), 4.15 (3H, s), 4.09 (3H, s), 4.04 (2H, t, J = 6.1 Hz), 2.25 (3H, d, J = 6.3 Hz), 2.08 (3H, d, J = 3.2 Hz), 2.13 - 2.20 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 522 (M⁺+1)

Example 154: 3-(4-Fluorophenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0256] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (68 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (94 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(4-fluorophenoxy)-1-propanol (54 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (68 mg, yield 58%).

¹H-NMR (CDCl₃, 400 MHz): 8.49 (1H, dd, J = 6.5 Hz), 8.10 (1H, s), 7.85 (1H, bs), 7.61 (1H, s), 6.78 - 6.97 (4H, m), 6.56 (1H, d, J = 6.3 Hz), 6.50 (1H, d, J = 6.8 Hz), 4.38 (1H, t, J = 6.3 Hz), 4.34 (1H, t, J = 6.3 Hz), 4.13 (3H, s), 4.13 (3H, s), 4.07 (3H, s), 4.04 (2H, t, J = 6.0 Hz), 2.25 (3H, d, J = 5.6 Hz), 2.09 (3H, d, J = 5.1 Hz)

Mass spectrometry value (ESI-MS, m/z): 522 (M⁺+1)

Example 155: 3-(4-Fluorophenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0257] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (59 mg) was added to toluene/triethylamine = 10/1 (6 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (89 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(4-fluorophenoxy)-1-propanol (51 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (51 mg, yield 49%).

¹H-NMR (CDCl₃, 400 MHz): 8.73 (1H, s), 7.97 (1H, s), 7.58 (1H, s), 7.53 - 7.57 (2H, m), 7.16 - 7.19 (2H, m), 6.89 - 6.98 (2H, m), 6.78 - 6.85 (2H, m), 4.37 (1H, t, J = 6.3 Hz), 4.34 (1H, t, J = 6.3 Hz), 4.14 (3H, s), 4.09 (3H, s), 4.03 (2H, t, J = 6.3 Hz), 2.08 - 2.20 (2H, m)

Mass spectrometry value (ESI-MS, m/z) : 494 (M⁺+1)

Example 156: 3-(4-Fluorophenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)-2,3-dimethylphenyl]carbamate

[0258] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2,3-dimethylaniline (68 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (94 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(4-fluorophenoxy)-1-propanol (53 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (48 mg, yield 41%).

¹H-NMR (CDCl₃, 400 MHz) : 8.71 (1H, s), 7.91 (1H, s), 7.66 (1H, bs), 7.61 (1H, s), 6.91 - 7.02 (3H, m), 6.78 - 6.84 (2H, m), 6.44 (1H, bs), 4.37 (1H, t, J = 6.5 Hz), 4.33 (1H, t, J = 6.5 Hz), 4.14 (3H, s), 4.10 (3H, s), 4.00 - 4.08 (2H, m), 2.23 (3H, d, J = 6.1 Hz), 2.06 (3H, d, J = 3.2 Hz), 2.10 - 2.20 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 523 (M⁺+1)

Example 157: 3-(2-Methoxyphenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolyloxy)phenyl]carbamate

[0259] 4-[(6,7-Dimethoxy-4-quinolyloxy)aniline (72 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (109 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(2-methoxyphenoxy)-1-propanol (66 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (91 mg, yield 69%).

¹H-NMR (CDCl₃, 400 MHz): 8.47 (1H, bs), 8.12 (1H, s), 7.61 (1H, s), 7.55 - 7.60 (2H, m), 7.13 - 7.18 (2H, m), 6.85 - 6.95 (4H, m), 6.68 (1H, bs), 4.42 (2H, t, J = 6.2 Hz), 4.12 - 4.20 (2H, m), 4.14 (3H, s), 4.08 (3H, s), 3.85 (3H, s), 2.17 - 2.26 (2H, m)

Mass spectrometry value (ESI-MS, m/z) : 5.06 (M+1)

Example 158: 3-(2-Methoxyphenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolyloxy)-2,3-dimethylphenyl]carbamate

[0260] 4-[(6,7-Dimethoxy-4-quinolyloxy)-2,3-dimethylaniline (70 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (97 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(2-methoxyphenoxy)-1-propanol (60 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound

(77 mg, yield 63%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 (1H, dd, J = 6.6 Hz), 8.14 (1H, d like, J = 4.1 Hz), 7.72 (1H, bs), 7.64 (1H, s), 6.99 (1H, d, J = 8.8 Hz), 6.86 - 6.96 (4H, m), 6.53 (1H, d, J = 6.6 Hz), 6.47 (1H, bs), 4.41 (2H, t, J = 6.3 Hz), 4.15 (3H, s), 4.15 (2H, t, J = 6.2 Hz), 4.09 (3H, s), 3.85 (3H, s), 2.24 (3H, s), 2.07 (3H, s), 2.19 - 2.26 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 534 (M⁺+1)

Example 159: 3-(2-Methoxyphenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0261] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (68 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (94 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(2-methoxyphenoxy)-1-propanol (60 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (61 mg, yield 51%).

¹H-NMR (CDCl₃, 400 MHz): 8.44 (1H, d, J = 6.4 Hz), 8.14 (1H, d like, J = 3.9 Hz), 7.87 (1H, bs), 6.87 - 6.97 (5H, m), 7.62 (1H, s), 6.56 (1H, d, J = 6.4 Hz), 6.43 (1H, bs), 4.42 (2H, t, J = 6.2 Hz), 4.15 (3H, s), 4.15 (2H, t, J = 6.2 Hz), 4.08 (3H, s), 3.85 (3H, s), 2.23 (2H, t, J = 6.2 Hz), 2.26 (3H, s), 2.10 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 534 (M⁺+1)

Example 160: 3-(2-Methoxyphenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)]phenyl}carbamate

[0262] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)]aniline (75 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (114 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(2-methoxyphenoxy)-1-propanol (69 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (51 mg, yield 35%).

¹H-NMR (CDCl₃, 400 MHz): 8.71 (1H, s), 8.04 (1H, s), 7.54 (1H, s), 7.46 - 7.53 (2H, m), 6.70 - 7.20 (7H, m), 4.36 (1H, t, J = 6.2 Hz), 4.30 (1H, t, J = 6.2 Hz), 4.12 (3H, s), 4.05 (3H, s), 4.05 - 4.11 (2H, m), 3.79 (3H, s), 2.10 - 2.20 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 507 (M⁺+1)

Example 161: 3-(3-Methoxyphenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0263] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (70 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (106 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(3-methoxyphenoxy)-1-propanol (64 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (69 mg, yield 54%).

¹H-NMR (CDCl₃, 400 MHz): 8.45 (1H, dd, J = 6.3 Hz), 8.13 (1H, d like, J = 3.9 Hz), 7.62 (1H, s), 7.55 - 7.65 (3H, m), 7.12 - 7.18 (3H, m), 6.65 - 6.75 (1H, m), 6.43 - 6.52 (1H, m), 6.44 - 6.47 (1H, m), 4.22 - 4.41 (2H, m), 4.14 (3H, s), 4.08 (3H, s), 4.05 - 4.14 (2H, m), 3.76 (3H, s), 2.14 - 2.20 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 506 (M⁺+1)

Example 162: 3-(3-Methoxyphenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0264] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (72 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (100 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(3-meth-

oxyphenoxy)-1-propanol (61 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (83 mg, yield 66%).

¹H-NMR (CDCl₃, 400 MHz): 8.39 (1H, d like, J = 6.7 Hz), 8.08 (1H, d like, J = 3.4 Hz), 7.60 - 7.70 (1H, m), 7.59 (1H, s), 7.11 (1H, dd, J = 8.2 Hz), 6.94 (1H, d, J = 9.0 Hz), 6.39 - 6.50 (4H, m), 4.34 (2H, t, J = 6.3 Hz), 4.09 (3H, s), 4.04 (3H, s), 4.01 (2H, t, J = 6.2 Hz), 3.72 (3H, s), 2.19 (3H, s), 2.08 - 2.15 (2H, m), 2.02 (3H, s)

Mass spectrometry value (ESI-MS, m/z) : 534 (M⁺+1)

Example 163: 3-(3-Methoxyphenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0265] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (73 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (101 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(3-methoxyphenoxy)-1-propanol (62 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (59 mg, yield 46%).

¹H-NMR (CDCl₃, 400 MHz): 8.45 - 8.55 (1H, m), 8.11 (1H, s), 7.86 (1H, s), 7.62 (1H, s), 7.16 (1H, dd, J = 8.2 Hz), 6.92 (1H, s), 6.56 (1H, d, J = 6.4 Hz), 6.40 - 6.52 (4H, m), 4.39 (2H, t, J = 6.2 Hz), 4.14 (3H, s), 4.08 (3H, s), 4.07 (2H, t, J = 6.4 Hz), 3.77 (3H, s), 2.26 (3H, s), 2.14 - 2.22 (2H, m), 2.10 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 534 (M⁺+1)

Example 164: 3-(3-Methoxyphenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinazolyl)oxy]phenyl}carbamate

[0266] 4-[(6,7-Dimethoxy-4-quinazolyl)oxy]aniline (75 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (114 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(3-methoxyphenoxy)-1-propanol (69 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (51 mg, yield 35%).

¹H-NMR (CDCl₃, 400 MHz): 8.71 (1H, s), 8.04 (1H, s), 7.54 (1H, s), 7.46 - 7.53 (2H, m), 6.70 - 7.20 (7H, m), 4.36 (1H, t, J = 6.2 Hz), 4.30 (1H, t, J = 6.2 Hz), 4.12 (3H, s), 4.05 (3H, s), 4.05 - 4.11 (2H, m), 3.79 (3H, s), 2.10 - 2.20 (2H, m)

Mass spectrometry value (ESI-MS, m/z): 507 (M⁺+1)

Example 165: 2-[(2,5-dimethylphenyl)sulfanyl]ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0267] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (77 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (105 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-[(2,5-dimethylphenyl)sulfanyl]-1-ethanol (78 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (105 mg, yield 74%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 - 8.48 (1H, m), 8.13 (1H, d like, J = 3.9 Hz), 7.62 (1H, s), 7.56 (2H, d, J = 9.0 Hz), 7.16 (2H, d, J = 9.0 Hz), 7.02 (2H, d, J = 9.0 Hz), 6.84 (1H, s), 6.76 (1H, s), 6.67 (1H, d, J = 6.6 Hz), 4.35 (2H, t, J = 6.6 Hz), 4.15 (3H, s), 4.08 (3H, s), 3.18 (2H, t, J = 6.6 Hz), 2.27 (6H, s)

Mass spectrometry value (ESI-MS, m/z): 506 (M⁺+1)

Example 166: 2-[(2,5-Dimethylphenyl)sulfanyl]ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl} carbamate

[0268] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (62 mg) was added to toluene/triethylamine = 10/1 (61 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (85 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-[(2,5-dimethylphenyl)sulfanyl]-1-ethanol (55 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (88 mg, yield 81%).

¹H-NMR (CDCl₃, 400 MHz): 8.44 (1H, d, J = 6.6 Hz), 8.14 (1H, s, J = 4.2 Hz), 7.72 (1H, bs), 7.64 (1H, s), 7.01 - 7.04 (2H, m), 6.99 (1H, s), 6.84 (1H, s), 6.53 (1H, d, J = 6.4 Hz), 6.43 (1H, s), 3.71 (1H, t, J = 6.0 Hz), 4.15 (3H, s), 4.09 (3H, s), 3.19 (2H, t, J = 6.0 Hz), 2.27 (6H, s), 2.23 (3H, s), 2.08 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 534 (M⁺+1)

Example 167: 2-[(2,5-Dimethylphenyl)sulfanyl]ethyl N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl} carbamate

[0269] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (68 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (97 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-[(2,5-dimethylphenyl)sulfanyl]-1-ethanol (60 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (79 mg, yield 66%).

¹H-NMR (CDCl₃, 400 MHz): 8.45 (1H, dd, J = 6.6 Hz), 8.13 (1H, d, J = 4.2 Hz), 7.86 (1H, s), 7.62 (1H, s), 7.02 (2H, s), 6.93 (1H, s), 6.84 (1H, s), 6.55 (1H, d, J = 6.6 Hz), 6.40 (1H, s), 4.36 (1H, t, J = 6.7 Hz), 4.15 (3H, s), 4.08 (3H, s), 3.20 (2H, t, J = 6.7 Hz), 2.27 (6H, s), 2.24 (3H, s), 2.11 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 534 (M⁺+1)

Example 168: 2-[(2,5-Dimethylphenyl)sulfanyl]ethyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)]phenyl}carbamate

[0270] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)]aniline (70 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (108 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-[(2,5-dimethylphenyl)sulfanyl]-1-ethanol (65 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (101 mg, yield 79%).

¹H-NMR (CDCl₃, 400 MHz): 8.77 (1H, s), 8.09 (1H, s), 7.59 (1H, s), 7.53 (2H, d, J = 9.0 Hz), 7.17 (2H, d, J = 8.8 Hz), 6.97 - 7.03 (2H, m), 6.72 - 6.85 (2H, m), 4.34 (2H, t, J = 6.6 Hz), 4.16 (3H, s), 4.10 (3H, s), 3.17 (2H, t, J = 6.6 Hz), 2.27 (6H, s)

Mass spectrometry value (ESI-MS, m/z): 507 (M⁺+1)

Example 169: 3-[(2,5-Dimethylphenyl)sulfanyl]propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0271] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (70 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (105 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-[(2,5-dimethylphenyl)sulfanyl]-1-propanol (78 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing

with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (48 mg, yield 37%).

¹H-NMR (CDCl₃, 400 MHz): 8.45 (1H, dd, J = 6.6 Hz), 8.12 (1H, s), 7.62 (1H, s), 7.56 - 7.61 (2H, m), 7.15 - 7.61 (2H, m), 7.15 - 7.25 (3H, m), 6.96 (1H, s), 6.80 - 6.80 - 6.85 (1H, m), 6.67 (1H, d, J = 6.4 Hz), 4.36 (1H, t, J = 6.4 Hz), 4.31 (1H, t, J = 6.4 Hz), 4.14 (3H, s), 4.08 (3H, s), 3.00 (2H, t, J = 7.1 Hz), 2.27 (6H, s), 1.97 - 2.25 (2H, m)

Mass spectrometry value (ESI-MS, m/z) : 520 (M⁺+1)

Example 170: 3-[(2,5-Dimethylphenyl)sulfanyl]propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl} carbamate

[0272] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (72 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (100 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-[(2,5-dimethylphenyl)sulfanyl]-1-propanol (60 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (33 mg, yield 25%).

¹H-NMR (CDCl₃, 400 MHz): 8.40 - 8.46 (1H, m), 8.14 (1H, s), 7.73 (1H, bs), 7.65 (1H, s), 6.94 - 7.02 (3H, m), 6.82 - 7.02 (3H, m), 6.82 (1H, s), 6.53 (1H, d, J = 6.6 Hz), 6.43 - 6.48 (1H, m), 4.28 - 4.37 (2H, m), 4.15 (3H, s), 4.09 (3H, s), 4.00 (2H, t, J = 7.1 Hz), 2.27 (6H, s), 2.25 (3H, s), 2.08 (3H, s), 1.98 - 2.20 (2H, m)

Mass spectrometry value (ESI-MS, m/z) : 548 (M⁺+1)

Example 171: 3-[(2,5-Dimethylphenyl)sulfanyl]propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl} carbamate

[0273] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (68 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (97 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-[(2,5-dimethylphenyl)sulfanyl]-1-propanol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (51 mg, yield 42%).

¹H-NMR (CDCl₃, 400 MHz): 8.41 - 8.45 (1H, m), 8.14 (1H, bs), 7.68 (1H, bs), 7.62 (1H, s), 6.97 (1H, s), 6.92 - 6.96 (1H, m), 6.82 (1H, s), 6.56 (1H, d, J = 6.6 Hz), 6.40 - 6.45 (1H, m), 4.36 (1H, t, J = 6.0 Hz), 4.32 (1H, t, J = 6.0 Hz), 3.00 (2H, t, J = 7.1 Hz), 2.27 (6H, s), 2.26 (3H, s), 2.14 - 2.20 (1H, m), 2.11 (3H, s), 1.98 - 2.05 (1H, m)

Mass spectrometry value (ESI-MS, m/z): 548 (M⁺+1)

Example 172: 3-[(2,5-Dimethylphenyl)sulfanyl]propyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)]phenyl}carbamate

[0274] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)]aniline (66 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (100 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-[(2,5-dimethylphenyl)sulfanyl]-1-propanol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (29 mg, yield 23%).

¹H-NMR (CDCl₃, 400 MHz): 8.75 (1H, s), 8.07 (1H, s), 7.59 (1H, s), 7.52 - 7.58 (2H, m), 6.79 - 7.21 (5H, m), 4.34 (1H, d, J = 6.1 Hz), 4.30 (1H, d, J = 6.1 Hz), 4.16 (3H, s), 4.10 (3H, s), 2.99 (2H, t, J = 7.1 Hz), 2.27 (6H, s), 2.11 - 2.19 (1H, m), 2.15 - 2.03 (1H, m)

Mass spectrometry value (ESI-MS, m/z): 521 (M⁺+1)

Example 173: 3-(2-Pyridylsulfanyl)propyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0275] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (111 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(2-pyridylsulfanyl)-1-propanol (63 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (18 mg, yield 13%).

¹H-NMR (CDCl₃, 400 MHz): 8.39 - 8.44 (2H, m), 7.90 - 7.95 (1H, m), 7.64 - 7.70 (1H, m), 7.63 (1H, s), 7.44 - 7.50 (1H, m), 7.15 - 7.20 (1H, m), 6.95 - 7.02 (2H, m), 6.42 - 6.48 (1H, m), 4.33 (2H, t, J = 6.2 Hz), 4.12 (3H, s), 4.08 (3H, s), 3.29 (2H, t, J = 7.1 Hz), 2.25 (3H, s), 2.09 - 2.15 (2H, m), 2.09 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 521 (M⁺+1)

Example 174: 3-(2-Pyridylsulfanyl)propyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0276] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (78 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (110 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(2-pyridylsulfanyl)-1-propanol (62 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (13 mg, yield 10%).

¹H-NMR (CDCl₃, 400 MHz): 8.75 - 8.79 (1H, m), 8.41 - 8.47 (1H, m), 8.12 (1H, s), 8.06 - 8.14 (1H, m), 7.99 (1H, bs), 7.81 (1H, s), 7.69 (1H, d, J = 8.5 Hz), 7.63 (1H, s like), 7.52 - 7.58 (1H, m), 6.92 (1H, s), 6.58 (1H, d, J = 6.3 Hz), 4.30 (2H, t, J = 5.6 Hz), 4.14 (3H, s), 4.09 (3H, s), 3.99 (2H, t, J = 7.3 Hz), 2.40 (3H, s), 2.08 - 2.22 (2H, m), 2.08 (3H, s)

Mass spectrometry value (ESI-MS, m/z) : 521 (M⁺+1)

Example 175: 3-(2-Pyridylsulfanyl)propyl N-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0277] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (73 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (110 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(2-pyridylsulfanyl)-1-propanol (62 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (5 mg, yield 4%).

Mass spectrometry value (ESI-MS, m/z) : 494 (M⁺+1)

Example 176: 4-Chloro-2-methylphenyl [4-[(6,7-dimethoxy-4-quinolyl)oxy]anilino]methanethioate

[0278] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (88 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (70 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-methyl-4-chlorophenol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (108 mg, yield 70%).

Mass spectrometry value (ESI-MS, m/z): 482 (M⁺+1)

Example 177: 4-Chloro-2-methylphenyl 4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylanilino}methanethioate

[0279] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (82 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (114 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-methyl-4-chlorothiophenol (60 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (91 mg, yield 66%).

Mass spectrometry value (ESI-MS, m/z): 510 (M⁺+1)

Example 178: 4-Chloro-2-methylphenyl 4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylanilino}methanethioate

[0280] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (79 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (110 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-methyl-4-chlorothiophenol (58 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (71 mg, yield 53%).

Mass spectrometry value (ESI-MS, m/z): 510 (M⁺+1)

Example 179: 4-Chloro-2-methylphenyl 4-[(6,7-dimethoxy-4-quinazolinyl)oxy]anilino}methanethioate

[0281] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (121 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-methyl-4-chlorothiophenol (64 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (68 mg, yield 49%).

Mass spectrometry value (ESI-MS, m/z): 493 (M⁺+1)

Example 180: 1-[3-(Trifluoromethoxy)phenyl]ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0282] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (82 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (124 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-trifluoromethoxy- α -methylbenzyl alcohol (85 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (61 mg, yield 39%).

¹H-NMR (CDCl₃, 400 MHz) : 8.39 (1H, dd, J = 6.6 Hz), 8.07 (1H, s like), 7.50 - 7.56 (2H, m), 7.31 - 7.36 (3H, m), 7.23 - 7.28 (1H, m), 7.08 - 7.13 (2H, m), 6.82 (1H, s), 6.60 (1H, d, J = 6.6 Hz), 5.85 (1H, q, J = 6.6 Hz), 4.09 (3H, s), 4.02 (3H, s), 1.55 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 529 (M⁺+1)

Example 181: 1-[3-(Trifluoromethoxy)phenyl]ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl} carbamate

[0283] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (88 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (122 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-trifluoromethoxy- α -methylbenzyl alcohol (83 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (73 mg, yield 46%).

¹H-NMR (CDCl₃, 400 MHz): 8.42 (1H, dd, J = 6.5 Hz), 8.13 (1H, s), 7.63 - 7.75 (2H, m), 6.96 - 7.42 (5H, m), 6.51 (2H, d, J = 6.5 Hz), 5.89 (1H, q, J = 6.6 Hz), 4.15 (3H, s), 4.09 (3H, s), 2.24 (3H, s), 2.07 (3H, s), 1.61 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 558 (M⁺+1)

Example 182: 1-[3-(Trifluoromethoxy)phenyl]ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl} carbamate

[0284] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (90 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (125 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-trifluoromethoxy- α -methylbenzyl alcohol (85 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (78 mg, yield 48%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 (1H, dd, J = 6.6 Hz), 8.13 (1H, s), 7.85 (1H, s), 7.62 (1H, s), 7.40 (1H, dd, J = 7.8 Hz), 7.31 (1H, d, J = 7.8 Hz), 7.16 (1H, d, J = 8.0 Hz), 6.93 (1H, s), 6.54 (1H, d, J = 6.6 Hz), 6.48 (1H, s), 5.89 (1H, q, J = 6.7 Hz), 4.15 (3H, s), 4.08 (3H, s), 2.27 (3H, s), 2.09 (3H, s), 1.62 (3H, d, J = 6.7 Hz)

Mass spectrometry value (ESI-MS, m/z) : 558 (M⁺+1)

Example 183: 1-[3-(Trifluoromethoxy)phenyl]ethyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0285] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (82 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (124 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-trifluoromethoxy- α -methylbenzyl alcohol (85 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (48 mg, yield 31%).

¹H-NMR (CDCl₃, 400 MHz) : 8.75 (1H, s), 8.11 (1H, s), 7.53 - 7.59 (3H, m), 7.38 (1H, dd, J = 7.9 Hz), 7.30 (1H, d, J = 7.9 Hz), 7.12 - 7.19 (3H, m), 6.87 (1H, s), 5.89 (1H, q, J = 6.6 Hz), 4.16 (3H, s), 4.10 (3H, s), 1.60 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 530 (M⁺+1)

Example 184: 1-Phenylbutyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0286] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (78 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (118 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 1-phenyl-1-butanol (59 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (78 mg, yield 58%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 (1H, dd, J = 6.6 Hz), 8.12 (1H, s like), 7.60 (1H, s), 7.53 - 7.58 (2H, m), 7.23 - 7.38 (4H, m), 7.12 - 7.15 (2H, m), 6.80 (1H, s), 6.64 (1H, d, J = 6.6 Hz), 5.72 - 5.78 (1H, m), 4.14 (3H, s), 4.07 (3H, s), 1.75 - 2.03 (2H, m), 1.35 - 1.45 (2H, m), 0.94 (2H, d, J = 7.3 Hz)

Mass spectrometry value (ESI-MS, m/z) : 474 (M⁺+1)

Example 185: 1-Phenylbutyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0287] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (90 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (125 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 1-phenyl-1-butanol (62 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (59 mg, yield 40%).

¹H-NMR (CDCl₃, 400 MHz): 8.36 (1H, dd, J = 6.5 Hz), 8.08 (1H, s), 7.67 (1H, d, J = 8.8 Hz), 7.59 (1H, s), 7.24 - 7.34 (5H, m), 6.92 (1H, d, J = 8.8 Hz), 6.42 - 6.47 (2H, m), 5.69 (1H, t, J = 6.9 Hz), 4.10 (3H, s), 4.04 (3H, s), 2.18 (3H, s), 2.01 (3H, s), 1.70 - 2.00 (2H, m), 1.2 - 1.42 (2H, m), 0.90 (3H, t, J = 7.4 Hz)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

Example 186: 1-Phenylbutyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0288] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (89 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (126 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 1-phenyl-1-butanol (63 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (58 mg, yield 39%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 (1H, dd, J = 6.5 Hz), 8.12 (1H, s like), 7.89 (1H, s), 7.61 (1H, s), 7.26 - 7.40 (5H, m), 6.91 (1H, s), 6.53 (1H, d, J = 6.5 Hz), 6.47 (1H, s), 5.71 - 5.76 (1H, m), 4.14 (3H, s), 4.08 (3H, s), 2.25 (3H, s), 2.07 (3H, s), 1.75 - 2.05 (2H, m), 1.25 - 1.50 (2H, m), 0.95 (3H, t, J = 7.3 Hz)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

Example 187: 1-Phenylbutyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0289] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (76 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (115 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 1-phenyl-1-butanol (57 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (38 mg, yield 29%).

¹H-NMR (CDCl₃, 400 MHz): 8.71 (1H, s), 8.07 (1H, s), 7.54 (1H, s), 7.44 - 7.52 (2H, m), 7.18 - 7.33 (5H, m), 7.08 - 7.13 (2H, m), 6.73 (1H, s), 5.65 - 5.72 (1H, m), 4.12 (3H, s), 4.05 (3H, s), 1.65 - 1.95 (2H, m), 1.30 - 1.40 (2H, m), 0.89 (3H, t, J = 7.4 Hz)

Mass spectrometry value (ESI-MS, m/z) : 475 (M⁺+1)

Example 188: 2-(Dimethylamino)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0290] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (83 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (40 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-dimethylaminoethanol (40 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion

of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (31 mg, yield 25%).

¹H-NMR (CDCl₃, 400 MHz): 8.41 (1H, d, J = 5.4 Hz), 7.56 - 7.65 (2H, m), 7.43 (1H, s), 7.20 - 7.26 (2H, m), 6.97 (1H, d, J = 8.8 Hz), 6.25 (1H, d, J = 5.1 Hz), 4.34 - 4.41 (2H, m), 4.05 (2H, s), 4.04 (3H, s), 2.92 (2H, bs), 2.57 (6H, bs)
Mass spectrometry value (ESI-MS, m/z): 412 (M⁺+1)

Example 189: 2-(Dimethylamino)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0291] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (111 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-dimethylaminoethanol (31 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (41 mg, yield 35%).

¹H-NMR (CDCl₃, 400 MHz): 8.41 (1H, d, J = 5.3 Hz), 7.59 (2H, s), 7.42 (1H, s), 6.96 (1H, d, J = 8.8 Hz), 6.24 (1H, d, J = 5.3 Hz), 4.30 - 4.38 (2H, m), 4.04 (3H, s), 4.03 (3H, s), 2.81 (2H, bs), 2.47 (6H, bs), 2.25 (3H, s), 2.09 (3H, s)
Mass spectrometry value (ESI-MS, m/z) : 441 (M⁺+1)

Example 190: 2-(Dimethylamino)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0292] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (85 mg) was added to toluene/triethylamine = 10/1 (9 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (115 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-dimethylaminoethanol (33 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (28 mg, yield 22%).

¹H-NMR (CDCl₃, 400 MHz):
Mass spectrometry value (ESI-MS, m/z) : 441 (M⁺+1)

Example 191: 2-(Dimethylamino)ethyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0293] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (74 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (112 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-dimethylaminoethanol (32 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (13 mg, yield 12%).

¹H-NMR (CDCl₃, 400 MHz): 8.42 (1H, m), 8.07 (1H, s), 7.10 - 7.70 (5H, m), 6.62 - 6.68 (1H, m), 4.47 - 4.52 (2H, m), 4.14 (3H, s), 4.08 (3H, s), 3.30 - 3.35 (2H, m), 2.94 (6H, s)
Mass spectrometry value (ESI-MS, m/z): 413 (M⁺+1)

Example 192: 4-(Dimethylamino)butyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0294] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (130 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-dimethylaminopropanol (40 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion

of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (22 mg, yield 17%).

Mass spectrometry value (ESI-MS, m/z): 441 ($M^{+1}+1$)

Example 193: 4-(Dimethylamino)butyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0295] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (76 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (106 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-dimethylaminopropanol (40 mg) was added thereto; and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (29 mg, yield 25%).

Mass spectrometry value (ESI-MS, m/z) : 469 ($M^{+1}+1$)

Example 194: 4-(Dimethylamino)butyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}carbamate

[0296] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (75 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (114 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 4-dimethylaminopropanol (43 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (18 mg, yield 15%).

Mass spectrometry value (ESI-MS, m/z): 413 ($M^{+1}+1$)

Example 195: 2-Methyl-1-phenylpropyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0297] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (77 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (118 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-methyl-1-phenyl-1-propanol (39 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (78 mg, yield 59%).

$^1\text{H-NMR}$ (CDCl_3 , 400 MHz): 8.40 - 8.45 (1H, m), 8.10 - 8.13 (1H, m), 7.10 - 7.61 (10H, m), 6.62 - 6.65 (1H, m), 5.45 (1H, d, $J = 7.8$ Hz), 4.14 (3H, s), 4.07 (3H, s), 2.00 - 2.25 (1H, m), 1.04 (3H, d, $J = 6.6$ Hz), 0.83 (3H, d, $J = 6.8$ Hz)

Mass spectrometry value (ESI-MS, m/z): 474 ($M^{+1}+1$)

Example 196: 2-Methyl-1-phenylpropyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0298] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution.. A solution of triphosgene (111 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-methyl-1-phenyl-1-propanol (55 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (69 mg, yield 52%).

¹H-NMR (CDCl₃, 400 MHz): 8.38 - 8.43 (1H, m), 8.11 - 8.15 (1H, m), 7.00 - 7.80 (8H, m), 6.95 - 7.00 (1H, m), 6.47 - 6.52 (1H, m), 5.45 (1H, d, J = 7.6 Hz), 4.14 (3H, s), 4.09 (3H, s), 2.23 (3H, s), 2.06 (3H, s), 2.00 - 2.25 (1H, m), 1.04 (3H, d, J = 6.6 Hz), 0.83 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

Example 197: 2-Methyl-1-phenylpropyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0299] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (124 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-methyl-1-phenyl-1-propanol (61 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (58 mg, yield 44%).

¹H-NMR (CDCl₃, 400 MHz): 8.39 - 8.44 (1H, m), 8.12 - 8.14 (1H, m), 7.85 - 7.90 (1H, s like), 7.61 (1H, s), 7.24 - 7.36 (5H, m), 6.91 (1H, s), 6.45 - 6.55 (2H, m), 5.45 (1H, d, J = 7.8 Hz), 4.14 (3H, s), 4.08 (3H, s), 2.26 (3H, s), 2.10 - 2.22 (1H, m), 2.07 (3H, s), 1.05 (3H, d, J = 6.6 Hz), 0.83 (3H, d, J = 6.8 Hz)

Mass spectrometry value (ESI-MS, m/z) : 502 (M⁺+1)

Example 198: 2-Methyl-1-phenylpropyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)]phenyl}carbamate

[0300] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)]aniline (75 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (137 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-methyl-1-phenyl-1-propanol (56 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (38 mg, yield 29%).

¹H-NMR (CDCl₃, 400 MHz): 8.72 (1H, s), 8.09 (1H, s), 7.58 (1H, s), 7.55 (2H, d, J = 8.8 Hz), 7.20 - 7.36 (5H, m), 7.13 - 7.16 (2H, m), 6.93 (1H, bs), 5.45 (1H, d, J = 7.6 Hz), 4.15 (3H, s), 4.09 (3H, s), 2.09 - 2.18 (1H, m), 1.02 (3H, d, J = 6.6 Hz), 0.82 (3H, d, J = 6.8 Hz)

Mass spectrometry value (ESI-MS, m/z): 475 (M⁺+1)

Example 199: 1-[3-(Dimethylamino)phenyl]ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0301] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (78 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-dimethylamino- α -methylbenzyl alcohol (65 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (61 mg, yield 44%).

¹H-NMR (CDCl₃, 400 MHz) : 8.39 (1H, d, J = 5.6 Hz), 7.42 - 7.57 (3H, m), 7.06 - 7.22 (2H, m), 6.54 - 6.74 (5H, m), 6.42 (1H, d, J = 5.6 Hz), 5.80 (1H, q, J = 6.6 Hz), 4.01 (3H, s), 3.99 (3H, s), 2.90 (3H, s), 2.89 (3H, s), 1.56 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 489 (M⁺+1)

Example 200: 1-[3-(Dimethylamino)phenyl]ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0302] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (83 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-dimeth-

ylamino- α -methylbenzyl alcohol (62 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (77 mg, yield 55%).

¹H-NMR (CDCl₃, 400 MHz): 8.41 (1H, d, J = 5.4 Hz), 7.48 - 7.65 (3H, m), 7.20 - 7.26 (1H, m), 6.96 (1H, d, J = 8.8 Hz), 6.65 - 6.78 (3H, m), 6.42 (1H, bs), 6.25 - 6.30 (1H, m), 5.85 (1H, q, J = 6.6 Hz), 4.04 - 4.06 (6H, m), 2.95 (6H, s), 2.22 (3H, s), 2.08 (3H, s), 1.61 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 517 (M⁺+1)

Example 201: 1-[3-(Dimethylamino)phenyl]ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0303] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (110 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-dimethylamino- α -methylbenzyl alcohol (60 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (58 mg, yield 43%).

[0304] ¹H-NMR (CDCl₃, 400 MHz) : 8.41 (1H, d, J = 5.6 Hz), 7.80 (1H, bs), 7.57 (1H, s), 7.55 (1H, bs), 7.20 - 7.26 (1H, m), 6.89 (1H, s), 6.72 - 6.79 (2H, m), 6.65 - 6.70 (1H, m), 6.41 (1H, bs), 6.31 (1H, q, J = 5.4 Hz), 5.85 (1H, q, J = 6.6 Hz), 4.05 (3H, s), 4.05 (3H, s), 2.96 (6H, s), 2.22 (3H, s), 2.10 (3H, s), 1.62 (3H, d, J = 6.6 Hz)

Mass spectrometry value (ESI-MS, m/z): 517 (M⁺+1)

Example 202: 1-[3-(Dimethylamino)phenyl]ethyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0305] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (120 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-dimethylamino- α -methylbenzyl alcohol (66 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (51 mg, yield 36%).

¹H-NMR (CDCl₃, 400 MHz): 8.54 (1H, s), 7.48 (1H, s), 7.42 (1H, d, J = 7.8 Hz), 7.25 (1H, s), 7.10 - 7.20 (3H, m), 6.58 - 6.74 (5H, m), 5.80 (1H, q, J = 6.5 Hz), 3.99 (3H, s), 3.99 (3H, s), 2.90 (6H, s), 1.55 (3H, d, J = 6.5 Hz)

Mass spectrometry value (ESI-MS, m/z): 490 (M⁺+1)

Example 203: 2-(2-Fluorophenoxy)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0306] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (60 mg) was added to toluene/triethylamine = 10/1 (6 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (91 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-(2-fluorophenoxy)-1-ethanol (47 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (52 mg, yield 50%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 - 8.49 (1H, m), 8.13 (1H, d, J = 3.9 Hz), 7.62 (1H, s), 7.59 (2H, d, J = 8.6 Hz), 7.17 (2H, d, J = 9.0 Hz), 6.90 - 7.12 (5H, m), 6.68 (1H, d, J = 6.1 Hz), 4.54 - 4.59 (2H, m), 4.28 - 4.33 (2H, m), 4.15 (3H, s), 4.08 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 479 (M⁺+1)

Example 204: 2-(2-Fluorophenoxy)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0307] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (62 mg) was added to toluene/triethylamine = 10/1 (6 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (86 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-(2-fluorophenoxy)-1-ethanol (45 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (49 mg, yield 47%).

¹H-NMR (CDCl₃, 400 MHz): 8.40 - 8.45 (1H, t, J = 6.5 Hz), 8.14 (1H, s like), 7.72 (1H, bs), 7.64 (1H, s), 6.90 - 7.12 (5H, m), 6.59 (1H, bs), 6.53 (1H, d, J = 6.4 Hz), 4.56 (2H, t, J = 4.6 Hz), 4.30 (2H, t, J = 4.6 Hz), 4.15 (3H, s), 4.09 (3H, s), 2.25 (3H, s), 2.08 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 508 (M⁺+1)

Example 205: 2-(2-Fluorophenoxy)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0308] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (55 mg) was added to toluene/triethylamine = 10/1 (6 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (76 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-(2-fluorophenoxy)-1-ethanol (40 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (61 mg, yield 66%).

¹H-NMR (CDCl₃, 400 MHz): 8.46 - 8.53 (1H, m), 8.11 (1H, d, J = 1.7 Hz), 7.85 (1H, bs), 7.62 (1H, s), 6.85 - 7.12 (5H, m), 6.54 - 6.64 (2H, m), 4.54 - 4.58 (2H, m), 4.29 - 4.32 (2H, m), 4.14 (3H, s), 4.08 (3H, s), 2.26 (3H, s), 2.10 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 508 (M⁺+1)

Example 206: 2-(2-Fluorophenoxy)ethyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0309] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene/triethylamine = 10/1 (5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (76 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-(2-fluorophenoxy)-1-ethanol (40 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (38 mg, yield 44%).

¹H-NMR (CDCl₃, 400 MHz): 8.75 (1H, s), 7.99 (1H, s), 7.59 (1H, s), 7.54 (2H, d, J = 8.8 Hz), 7.19 (2H, d, J = 9.0 Hz), 6.85 - 7.12 (5H, m), 4.53 - 4.56 (2H, m), 4.28 - 4.32 (2H, m), 4.15 (3H, s), 4.09 (3H, s)

Mass spectrometry value (ESI-MS, m/z) : 480 (M⁺+1)

Example 207: 2-(3-Fluorophenoxy)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0310] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (62 mg) was added to toluene/triethylamine = 10/1 (6 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (92 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-(3-fluorophenoxy)-1-ethanol (48 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (55 mg, yield 51%).

¹H-NMR (CDCl₃, 400 MHz): 8.43 - 8.49 (1H, m), 8.10 - 8.13 (1H, m), 7.57 - 7.64 (3H, m), 6.60 - 7.25 (7H, m),

4.52 - 4.57 (2H, m), 4.18 - 4.27 (2H, m), 4.14 (3H, s), 4.08 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 479 (M⁺+1)

Example 208: 2-(3-Fluorophenoxy)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0311] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (70 mg) was added to toluene/triethylamine = 10/1 (7 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (97 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-(3-fluorophenoxy)-1-ethanol (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (78 mg, yield 67%).

¹H-NMR (CDCl₃, 400 MHz): 8.42 - 8.49 (1H, m), 8.12 - 8.14 (1H, m), 7.73 (1H, bs), 7.64 (1H, s), 7.21 (1H, d, J = 8.0 Hz), 7.00 (1H, d, J = 8.8 Hz), 6.50 - 6.74 (4H, m), 4.54 (2H, t, J = 4.5 Hz), 4.21 (2H, t, J = 4.5 Hz), 4.15 (3H, s), 4.09 (3H, s), 2.25 (3H, s), 2.08 (3H, s)

Mass spectrometry value (ESI-MS, m/z) : 508 (M⁺+1)

Example 209: 2-(3-Fluorophenoxy) ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0312] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (56 mg) was added to toluene/triethylamine = 10/1 (6 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (78 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-(3-fluorophenoxy)-1-ethanol (40 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (54 mg, yield 57%).

¹H-NMR (CDCl₃, 400 MHz): 8.40 - 8.50 (1H, m), 8.11 (1H, s), 8.00 (1H, s), 7.84 - 7.91 (1H, m), 7.60 - 7.67 (2H, m), 6.40 - 6.99 (5H, m), 4.08 - 4.28 (4H, m), 4.14 (3H, s), 4.09 (3H, s), 2.26 (3H, s), 2.11 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 508 (M⁺+1)

Example 210: 2-(3-Fluorophenoxy)ethyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0313] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (55 mg) was added to toluene/triethylamine = 10/1 (6 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (83 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 2-(3-fluorophenoxy)-1-ethanol (43 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (28 mg, yield 29%).

¹H-NMR (CDCl₃, 400 MHz): 8.75 (1H, m), 8.05 (1H, s like), 7.59 (1H, s), 7.50 - 7.58 (2H, m), 7.17 - 7.24 (2H, m), 6.60 - 6.73 (4H, m), 4.52 - 4.56 (2H, m), 4.19 - 4.23 (2H, m), 4.16 (3H, s), 4.10 (3H, s)

Mass spectrometry value (ESI-MS, m/z): 480 (M⁺+1)

Example 211: 3-(2-Chlorophenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2,3-dimethylphenyl}carbamate

[0314] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2,3-aniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (111 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(2-chlorophenoxy)-1-propanol (69 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was

concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (70 mg, yield 50%).

¹H-NMR (CDCl₃, 400 MHz): 8.74 (1H, d, J = 1.7 Hz), 8.08 (1H, s), 7.70 (1H, bs), 7.62 (1H, s), 7.32 - 7.36 (1H, m), 7.17 - 7.22 (1H, m), 7.00 (1H, dd, J = 6.8 Hz, J = 9.3 Hz), 6.85 - 6.95 (2H, m), 6.44 (1H, bs), 4.43 (1H, t, J = 6.2 Hz), 4.34 (1H, t, J = 6.2 Hz), 4.10 - 4.20 (1H, m), 4.18 (3H, s), 4.11 (3H, s), 3.60 - 3.70 (1H, m), 2.23 (1H, d, J = 5.9 Hz), 2.06 (1H, d, J = 4.1 Hz), 2.08 - 2.22 (2H, m)

Mass spectrometry value (ESI-MS, m/z) : 539 (M⁺+1)

Example 212: 3-(3-Chlorophenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2,3-dimethylphenyl}carbamate

[0315] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2,3-aniline (80 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (111 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(3-chlorophenoxy)-1-propanol (62 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (65 mg, yield 46%).

¹H-NMR (CDCl₃, 400 MHz): 8.75 (1H, d, J = 2.7 Hz), 8.14 (1H, s), 7.70 (1H, bs), 7.62 (1H, s), 7.15 - 7.22 (1H, m), 6.97 - 7.03 (1H, m), 6.87 - 6.95 (1H, m), 6.76 - 6.82 (1H, m), 6.42 (1H, bs), 4.32 - 4.39 (2H, m), 4.18 (3H, s), 4.11 (3H, s), 4.03 - 4.08 (1H, m), 3.62 - 3.68 (1H, m), 2.23 - 2.26 (3H, m), 2.12 - 2.21 (2H, m), 2.05 - 2.07 (3H, m)

Mass spectrometry value (ESI-MS, m/z): 539 (M⁺+1)

Example 213: 3-(4-Chlorophenoxy)propyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2,3-dimethylphenyl}carbamate

[0316] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2,3-aniline (82 mg) was added to toluene/triethylamine = 10/1 (8 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (114 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 15 min. Subsequently, 3-(4-chlorophenoxy)-1-propanol (71 mg) was added thereto, and the mixture was further stirred with heating under reflux for 2 hr. After the completion of the reaction, the reaction solution was allowed to cool to room temperature before distilled water was added thereto. The mixture was subjected to separatory extraction with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution and saturated brine. The washed solution was dried over sodium sulfate and was concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (85 mg, yield 59%).

¹H-NMR (CDCl₃, 400 MHz): 8.74 (1H, s like), 8.09 (1H, s), 7.69 (1H, bs), 7.62 (1H, s), 7.19 - 7.23 (2H, m), 7.97 - 7.02 (1H, m), 6.79 - 6.84 (2H, m), 6.42 (1H, bs), 4.32 - 4.39 (2H, m), 4.17 (3H, s), 4.11 (3H, s), 4.02 - 4.09 (2H, m), 2.23 - 2.26 (3H, m), 2.10 - 2.20 (2H, m), 2.05 - 2.07 (3H, m)

Mass spectrometry value (ESI-MS, m/z): 539 (M⁺+1)

Example 214: 3-Methoxyphenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0317] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (150 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 10 min. Next, 3-methoxyphenol (55 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (108 mg, yield 68%)

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.29 (s, 3H), 4.07 (s, 3H), 4.09 (s, 3H), 6.54 (brs, 1H), 7.13 - 7.29 (m, 8H), 7.59 - 7.60 (m, 3H), 8.49 (d, J = 5.9 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 447 (M⁺+1)

Example 215: Propyl N-{4-[(6,7-Dimethoxy-4-quinolin)oxy]-2,3-dimethylphenyl}carbamate

[0318] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (138 mg) in

methylene chloride was then added to the solution, and the mixture was heated under reflux for 10 min. Next, 1-propanol (28 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (120 mg, yield 87%).

¹H-NMR (DMSO-d₆, 400 MHz) : δ 0.95 (t, J = 7.6 Hz, 3H), 1.63 - 1.66 (m, 2H), 2.07 (s, 3H), 2.20 (s, 3H), 4.04 (t, J = 6.8 Hz, 2H), 4.05 (s, 6H), 6.67 (d, J = 6.6 Hz, 1H), 7.15 (d, J = 8.3 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 7.60 (s, 1H), 7.79 (s, 1H), 8.77 (d, J = 6.6 Hz, 1H), 9.06 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 411 (M⁺+1)

Example 216: Phenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0319] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 10 min. Next, phenol (48 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (97 mg, yield 63%).

¹H-NMR (DMSO-d₆, 400 MHz) : δ 4.03 (s, 3H), 4.04 (s, 3H), 6.83 (d, J = 6.3 Hz, 1H), 7.24 - 7.30 (m, 3H), 7.38 - 7.47 (m, 3H), 7.57 (s, 1H), 7.72 - 7.74 (m, 3H), 8.79 (d, J = 6.6 Hz, 1H), 10.50 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 417 (M⁺+1)

Example 217: Phenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0320] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (139 mg) in methylene chloride was then added to the solution, and the mixture was heated under reflux for 10 min. Next, phenol (44 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (73 mg, yield 49%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.10 (s, 3H), 2.30 (s, 3H), 4.05 (s, 6H), 6.69 (d, J = 6.6 Hz, 1H), 7.15 - 7.28 (m, 4H), 7.42 - 7.48 (m, 3H), 7.61 (s, 1H), 7.79 (s, 1H), 8.76 (d, J = 6.3 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 445 (M⁺+1)

Example 218: Benzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0321] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, phenylmethanol (51 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (137 mg, yield 89%).

¹H-NMR (CDCl₃-d₁, 400 MHz) : δ 2.13 (s, 3H), 2.27 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.24 (s, 2H), 6.52 (s, 1H), 6.59 (brs, 1H), 6.95 (s, 1H), 7.26 - 7.45 (m, 5H), 7.64 (s, 1H), 7.93 (s, 1H), 8.14 (s, 1H), 8.51 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 459 (M⁺+1)

Example 219: Benzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0322] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, phenylmethanol

(51 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (120 mg, yield 78%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.10 (s, 3H), 2.26 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.24 (s, 2H), 6.55 (s, 2H), 7.03 (d, J = 8.8 Hz, 1H), 7.37 - 7.43 (m, 5H), 7.67 (s, 1H), 7.76 (brs, 1H), 8.15 (s, 1H), 8.50 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 459 (M⁺+1)

Example 220: Benzyl N-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0323] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, phenylmethanol (55 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (100 mg, yield 58%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 4.12 (s, 3H), 4.19 (s, 3H), 5.23 (s, 2H), 6.96 (s, 1H), 7.19 (d, J = 9.0 Hz, 2H), 7.35 - 7.43 (m, 5H), 7.59 (d, J = 8.8 Hz, 2H), 7.61 (s, 1H), 8.14 (s, 1H), 8.79 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 432 (M⁺+1)

Example 221: Cyclohexyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0324] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cyclohexanol (47 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (80 mg, yield 53%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.49 - 1.57 (m, 10H), 1.76 - 1.80 (m, 2H), 1.97 - 2.01 (m, 2H), 2.13 (s, 3H), 2.29 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 6.39 (s, 1H), 6.59 (d, J = 9.0 Hz, 1H), 6.94 (s, 1H), 7.65 (s, 1H), 7.95 (s, 1H), 8.15 (s, 1H), 8.49 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 451 (M⁺+1)

Example 222: Cyclohexyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0325] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cyclohexanol (47 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (85 mg, yield 56%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.47 - 2.20 (m, 13H), 2.28 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.74 (brs, 1H), 6.43 (s, 1H), 6.57 (brs, 1H), 7.02 (d, J = 8.8 Hz, 1H), 7.67 (s, 1H), 7.75 (brs, 1H), 8.14 (s, 1H), 8.49 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 451 (M⁺+1)

Example 223: 2-Methylphenyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]carbamate

[0326] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, o-cresol (55 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution

was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (116 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 432 (M⁺+1)

Example 224: Phenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0327] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2, 5-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, phenol (44 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (69 mg, yield 50%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.15 (s, 3H), 2.34 (s, 3H), 4.01 (s, 3H), 4.07 (s, 3H), 6.32 (d, J = 5.4 Hz, 1H), 6.77 (brs, 1H), 6.97 (s, 1H), 7.22 - 7.28 (m, 3H), 7.40 - 7.47 (m, 3H), 7.60 (s, 1H), 7.85 (brs, 1H), 8.46 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 445 (M⁺+1)

Example 225: Benzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}carbamate

[0328] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (134 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, phenylmethanol (49 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (100 mg, yield 72%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 4.00 (s, 6H), 5.17 (s, 2H), 7.12 - 7.37 (m, 9H), 7.44 (s, 1H), 8.24 (d, J = 8.8 Hz, 1H), 8.56 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 467 (M⁺+1)

Example 226: 3-Methoxybenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0329] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (3-methoxyphenyl)methanol (71 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (133 mg, yield 79%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.83 (s, 3H), 4.10 (s, 3H), 4.17 (s, 3H), 5.21 (s, 2H), 6.58 (brs, 1H), 6.88 - 7.01 (m, 4H), 7.18 (d, J = 8.8 Hz, 1H), 7.29 - 7.33 (m, 1H), 7.61 - 7.63 (m, 3H), 8.14 (s, 1H), 8.50 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 462 (M⁺+1)

Example 227: 2-Chlorobenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0330] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-chlorophenyl)methanol (73 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (153 mg, yield 90%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 4.03 (s, 3H), 4.04 (s, 3H), 5.27 (s, 2H), 6.83 (d, J = 6.6 Hz, 1H), 7.35 (d, J = 9.0 Hz, 2H), 7.41 - 7.43 (m, 2H), 7.52 - 7.54 (m, 1H), 7.58 - 7.61 (m, 2H), 7.69 (d, J = 8.8 Hz, 2H), 7.74 (s, 1H), 8.77 (d, J = 6.6 Hz, 1H), 10.12 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 466 (M⁺+1)

Example 228: 3-Chlorobenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0331] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (3-chlorophenyl)methanol (73 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (158 mg, yield 93%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 4.03 (s, 3H), 4.04 (s, 3H), 5.20 (s, 2H), 6.82 (d, J = 6.6 Hz, 1H), 7.35 (d, J = 9.0 Hz, 2H), 7.42 - 7.47 (m, 3H), 7.52 (s, 1H), 7.63 (s, 1H), 7.69 (d, J = 9.0 Hz, 2H), 7.74 (s, 1H), 8.78 (d, J = 6.6 Hz, 1H), 10.09 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 466 (M⁺+1)

Example 229: 4-Chlorobenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0332] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (4-chlorophenyl)methanol (73 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (147 mg, yield 86%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 4.03 (s, 3H), 4.04 (s, 3H), 5.18 (s, 2H), 6.82 (d, J = 6.6 Hz, 1H), 7.35 (d, J = 9.0 Hz, 2H), 7.48 (s, 4H), 7.64 (s, 1H), 7.68 (d, J = 8.8 Hz, 2H), 7.74 (s, 1H), 8.78 (d, J = 6.6 Hz, 1H), 10.07 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 466 (M⁺+1)

Example 230: Cyclohexyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0333] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cyclohexanol (51 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (120 mg, yield 77%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.24 - 1.58 (m, 6H), 1.73 - 1.76 (m, 2H), 1.90 - 1.94 (m, 2H), 4.02 (s, 3H), 4.04 (s, 3H), 4.54 (brs, 1H), 6.79 (d, J = 6.3 Hz, 1H), 7.32 (d, J = 9.0 Hz, 2H), 7.55 (s, 1H), 7.67 (d, J = 9.0 Hz, 2H), 7.72 (s, 1H), 8.76 (d, J = 6.6 Hz, 1H), 9.82 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 423 (M⁺+1)

Example 231: Benzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0334] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, phenylmethanol (55 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to

give the title compound (130 mg, yield 82%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 4.03 (s, 3H), 4.04 (s, 3H), 5.19 (s, 2H), 6.82 (d, J = 6.6 Hz, 1H), 7.30 - 7.46 (m, 7H), 7.62 (s, 1H), 7.69 (d, J = 9.0 Hz, 2H), 7.74 (s, 1H), 8.78 (d, J = 6.6 Hz, 1H), 10.04 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 431 (M⁺+1)

Example 232: 2-Methylbenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0335] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-methylphenyl) methanol (57 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (140 mg, yield 89%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.07 (s, 3H), 2.20 (s, 3H), 2.36 (s, 3H), 4.05 (s, 6H), 5.17 (s, 2H), 6.67 (d, J = 6.6 Hz, 1H), 7.13 - 7.27 (m, 4H), 7.39 (d, J = 9.0 Hz, 2H), 7.62 (s, 1H), 7.79 (s, 1H), 8.76 (d, J = 6.6 Hz, 1H), 9.22 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 473 (M⁺+1)

Example 233: 3-Methylbenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0336] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (3-methylphenyl) methanol (57 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (140 mg, yield 89%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.07 (s, 3H), 2.20 (s, 3H), 2.33 (s, 3H), 4.05 (s, 6H), 5.12 (s, 2H), 6.65 (d, J = 6.8 Hz, 1H), 7.12 - 7.31 (m, 5H), 7.39 (d, J = 8.8 Hz, 2H), 7.60 (s, 1H), 7.78 (s, 1H), 8.75 (d, J = 6.8 Hz, 1H), 9.21 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 473 (M⁺+1)

Example 234: 4-Methylbenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0337] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (4-methylphenyl) methanol (57 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (40 mg, yield 25%).

¹H-NMR (CDCl₃-d₁, 400 MHz) : δ 2.07 (s, 3H), 2.19 (s, 3H), 2.32 (s, 3H), 4.04 (s, 6H), 5.11 (s, 2H), 6.65 (d, J = 6.3 Hz, 1H), 7.14 - 7.22 (m, 3H), 7.32 (d, J = 8.1 Hz, 2H), 7.38 (d, J = 8.8 Hz, 1H), 7.56 (s, 1H), 7.78 (s, 1H), 8.75 (d, J = 6.3 Hz, 1H), 9.19 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 473 (M⁺+1)

Example 235: 2-Chlorobenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0338] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-chlorophenyl) methanol (67 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (127 mg, yield 77%).

$^1\text{H-NMR}$ ($\text{CDCl}_3\text{-d}_1$, 400 MHz): δ 2.10 (s, 3H), 2.27 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.36 (s, 2H), 6.55 - 6.56 (m, 2H), 7.03 (d, $J = 9.0$ Hz, 1H), 7.25 - 7.33 (m, 1H), 7.43 - 7.50 (m, 2H), 7.67 (s, 1H), 8.15 (s, 1H), 8.48 (s, 1H)
Mass spectrometry value (ESI-MS, m/z): 494 ($M^+ + 1$)

5 Example 236: 3-Chlorobenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0339] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (3-chlorophenyl) methanol (67 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (147 mg, yield 90%).

15 $^1\text{H-NMR}$ ($\text{CDCl}_3\text{-d}_1$, 400 MHz): δ 2.10 (s, 3H), 2.27 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.21 (s, 2H), 6.56 (d, $J = 6.3$ Hz, 2H), 7.03 (d, $J = 8.5$ Hz, 1H), 7.25 - 7.35 (m, 3H), 7.43 (s, 1H), 7.67 (s, 1H), 7.75 (brs, 1H), 8.15 (s, 1H), 8.49 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 494 ($M^+ + 1$)

20 Example 237: 4-Chlorobenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0340] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (4-chlorophenyl) methanol (67 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (103 mg, yield 63%).

30 $^1\text{H-NMR}$ ($\text{CDCl}_3\text{-d}_1$, 400 MHz): δ 2.10 (s, 3H), 2.26 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.20 (s, 2H), 6.54 (brs, 2H), 7.03 (d, $J = 8.8$ Hz, 1H), 7.38 (s, 4H), 7.66 (s, 1H), 7.71 (brs, 1H), 8.15 (s, 1H), 8.50 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 494 ($M^+ + 1$)

35 Example 238: 3-Methoxybenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0341] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (3-methoxyphenyl)methanol (65 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (136 mg, yield 84%).

45 $^1\text{H-NMR}$ ($\text{CDCl}_3\text{-d}_1$, 400 MHz): δ 2.10 (s, 3H), 2.26 (s, 3H), 3.84 (s, 3H), 4.11 (s, 3H), 4.18 (s, 3H), 5.21 (s, 2H), 6.55 (brs, 2H), 6.84 - 7.02 (m, 4H), 7.25 - 7.32 (m, 1H), 7.67 (s, 1H), 7.83 (brs, 1H), 8.16 (s, 1H), 8.44 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 489 ($M^+ + 1$)

Example 239: 2-Methoxybenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

50 [0342] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-methoxyphenyl)methanol (65 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (130 mg, yield 80%).

$^1\text{H-NMR}$ ($\text{CDCl}_3\text{-d}_1$, 400 MHz): δ 2.13 (s, 3H), 2.26 (s, 3H), 3.90 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.31 (s, 2H),

6.51 (s, 1H), 6.58 (d, J = 6.6 Hz, 1H), 6.88 - 7.01 (m, 3H), 7.34 - 7.42 (m, 2H), 7.64 (s, 1H), 7.96 (s, 1H), 8.15 (s, 1H), 8.47 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 489 (M⁺+1)

5 Example 240: 3-Methoxybenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0343] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (3-methoxyphenyl)methanol (65 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (120 mg, yield 74%).

15 ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.13 (s, 3H), 2.27 (s, 3H), 3.84 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.22 (s, 2H), 6.51 (s, 1H), 6.58 (d, J = 6.3 Hz, 1H), 6.91 - 7.03 (m, 4H), 7.25 - 7.35 (m, 1H), 7.64 (s, 1H), 7.93 (s, 1H), 8.15 (s, 1H), 8.47 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 489 (M⁺+1)

20 Example 241: 2-Chlorobenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0344] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-chlorophenyl)methanol (67 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (112 mg, yield 68%).

30 ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.13 (s, 3H), 2.28 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.36 (s, 2H), 6.54 (s, 1H), 6.58 (d, J = 6.3 Hz, 1H), 6.96 (s, 1H), 7.26 - 7.33 (m, 2H), 7.43 - 7.49 (m, 2H), 7.64 (s, 1H), 7.93 (s, 1H), 8.15 (s, 1H), 8.47 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 494 (M⁺+1)

35 Example 242: 3-Chlorobenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0345] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (3-chlorophenyl)methanol (67 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (117 mg, yield 71%).

45 ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.14 (s, 3H), 2.29 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.21 (s, 2H), 6.53 (s, 1H), 6.56 (s, 1H), 6.96 (s, 1H), 7.26 - 7.38 (m, 3H), 7.44 (s, 1H), 7.64 (s, 1H), 7.91 (s, 1H), 8.15 (s, 1H), 8.43 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 494 (M⁺+1)

50 Example 243: 4-Chlorobenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0346] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (4-chlorophenyl)methanol (67 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (154 mg, yield 94%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.13 (s, 3H), 2.27 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.20 (s, 2H), 6.50 (s, 1H), 6.58 (s, 1H), 6.95 (s, 1H), 7.38 (s, 4H), 7.64 (s, 1H), 7.90 (s, 1H), 8.15 (s, 1H), 8.47 (brs, 1H)
Mass spectrometry value (ESI-MS, m/z) : 494 (M⁺+1)

5 Example 244: Propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0347] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-propanol (28 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (115 mg, yield 83%).

15 ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.01 (t, J = 7.3 Hz, 3H), 1.72 - 1.77 (m, 2H), 2.13 (s, 3H), 2.29 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.17 (t, J = 7.8 Hz, 2H), 6.42 (s, 1H), 6.60 (brs, 1H), 6.95 (s, 1H), 7.65 (s, 1H), 7.92 (s, 1H), 8.15 (s, 1H), 8.50 (brs, 1H)
Mass spectrometry value (ESI-MS, m/z): 411 (M⁺+1)

20 Example 245: 2-Methylbenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0348] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-methylphenyl) methanol (57 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (140 mg, yield 89%).

30 ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.13 (s, 3H), 2.26 (s, 3H), 2.43 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.27 (s, 2H), 6.50 (s, 1H), 6.58 (brs, 1H), 6.95 (s, 1H), 7.25 - 7.30 (m, 3H), 7.40 (d, J = 7.1 Hz, 1H), 7.64 (s, 1H), 7.94 (s, 1H), 8.15 (s, 1H), 8.50 (brs, 1H)
Mass spectrometry value (ESI-MS, m/z): 473 (M⁺+1)

35 Example 246: 2-Naphthylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0349] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-naphthylmethanol (87 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (160 mg, yield 90%).

45 ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.14 (s, 3H), 2.28 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.29 (s, 2H), 6.53 (s, 1H), 6.58 (s, 1H), 6.95 (s, 1H), 7.37 - 7.53 (m, 4H), 7.59 - 7.65 (m, 4H), 7.95 (s, 1H), 8.15 (s, 1H), 8.50 (brs, 1H)
Mass spectrometry value (ESI-MS, m/z) : 510 (M⁺+1)

50 Example 247: Propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0350] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-propanol (31 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (104 mg, yield 73%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.01 (t, J = 7.6 Hz, 3H), 1.71 - 1.76 (m, 2H), 4.10 (s, 3H), 4.17 (s, 3H), 4.17 (t, J = 8.1 Hz, 2H), 6.69 (brs, 1H), 6.81 (s, 1H), 7.18 (d, J = 8.8 Hz, 2H), 7.61 (d, J = 8.3 Hz, 2H), 7.64 (s, 1H), 8.14 (s, 1H), 8.50 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 383 (M⁺+1)

Example 248: 2-Methoxybenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0351] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-methoxyphenyl)methanol (71 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (123 mg, yield 73%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.89 (s, 3H), 4.10 (s, 3H), 4.17 (s, 3H), 5.30 (s, 2H), 6.69 (d, J = 6.3 Hz, 1H), 6.83 (s, 1H), 6.93 - 7.00 (m, 2H), 7.18 - 7.52 (m, 4H), 7.59 - 7.63 (m, 3H), 8.15 (s, 1H), 8.49 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 462 (M⁺+1)

Example 249: 4-Methoxybenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0352] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (4-methoxyphenyl)methanol (71 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (140 mg, yield 83%).

¹H-NMR (CDCl₃-d₁, 400 MHz) : δ 3.83 (s, 3H), 4.10 (s, 3H), 4.17 (s, 3H), 5.17 (s, 2H), 6.68 (d, J = 6.3 Hz, 1H), 6.83 (s, 1H), 6.92 (d, J = 8.5 Hz, 2H), 7.17 (d, J = 9.0 Hz, 2H), 7.37 (d, J = 8.5 Hz, 2H), 7.59 (d, J = 9.0 Hz, 2H), 7.63 (s, 1H), 8.14 (s, 1H), 8.49 (t, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 462 (M⁺+1)

Example 250: 2-Methylbenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0353] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-methylphenyl)methanol (62 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (143 mg, yield 88%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.42 (s, 3H), 4.10 (s, 3H), 4.17 (s, 3H), 5.27 (s, 2H), 6.68 (d, J = 6.3 Hz, 1H), 6.87 (s, 1H), 7.17 - 7.28 (m, 5H), 7.38 (d, J = 7.1 Hz, 1H), 7.61 (d, J = 9.0 Hz, 2H), 7.63 (s, 1H), 8.14 (s, 1H), 8.49 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 446 (M⁺+1)

Example 251: 3-Methylbenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0354] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (3-methylphenyl)methanol (62 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (146 mg, yield 89%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.38 (s, 3H), 4.10 (s, 3H), 4.17 (s, 3H), 5.20 (s, 2H), 6.69 (brs, 1H), 6.92 (s, 1H), 7.17 - 7.31 (m, 6H), 7.61 - 7.63 (m, 3H), 8.14 (s, 1H), 8.51 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 446 (M⁺+1)

5 Example 252: 4-Methylbenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0355] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (4-methylphenyl)methanol (62 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (133 mg, yield 81%).

15 ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.37 (s, 3H), 4.10 (s, 3H), 4.17 (s, 3H), 5.20 (s, 2H), 6.69 (brs, 1H), 6.92 (s, 1H), 7.16 - 7.33 (m, 6H), 7.60 (d, J = 7.3 Hz, 2H), 7.64 (s, 1H), 8.15 (s, 1H), 8.49 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 446 (M⁺+1)

20 Example 253: 2-Methylbenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0356] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethyl-aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-methylphenyl)methanol (57 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (122 mg, yield 77%).

30 ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.26 (s, 3H), 2.43 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.27 (s, 2H), 6.52 (s, 1H), 6.58 (d, J = 6.3 Hz, 1H), 6.95 (s, 1H), 7.24 - 7.30 (m, 3H), 7.40 (d, J = 7.1 Hz, 1H), 7.65 (s, 1H), 7.93 (s, 1H), 8.15 (s, 1H), 8.49 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 474 (M⁺+1)

35 Example 254: 3-Methylbenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0357] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethyl-aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (3-methylphenyl)methanol (57 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (120 mg, yield 76%).

45 ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.13 (s, 3H), 2.27 (s, 3H), 2.39 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.21 (s, 2H), 6.53 (s, 1H), 6.58 (brs, 1H), 6.95 (s, 1H), 7.18 - 7.30 (m, 4H), 7.64 (s, 1H), 7.94 (s, 1H), 8.15 (s, 1H), 8.48 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 474 (M⁺+1)

Example 255: 4-Methylbenzyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

50 [0358] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (4-methylphenyl)methanol (57 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (139 mg, yield 88%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.13 (s, 3H), 2.26 (s, 3H), 2.38 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.20 (s, 2H),

6.49 (s, 1H), 6.58 (brs, 1H), 6.94 (s, 1H), 7.22 (d, J = 7.8 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.64 (s, 1H), 7.94 (s, 1H), 8.15 (s, 1H), 8.50 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 474 (M⁺+1)

5 Example 256: Hexyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0359] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-hexanol (52 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (110 mg, yield 70%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.92 (t, J = 6.8 Hz, 3H), 1.33 - 1.35 (m, 6H), 1.67 - 1.72 (m, 2H), 4.10 (s, 3H), 4.17 (s, 3H), 4.20 (t, J = 6.8 Hz, 2H), 6.70 (d, J = 6.3 Hz, 1H), 6.79 (s, 1H), 7.18 (d, J = 9.0 Hz, 2H), 7.60 (d, J = 8.8 Hz, 2H), 7.64 (s, 1H), 8.14 (s, 1H), 8.51 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 426 (M⁺+1)

20 Example 257: 4-Butylphenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0360] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-butylphenol (77 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (130 mg, yield 75%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.94 (t, J = 7.3 Hz, 3H), 1.34 - 1.40 (m, 2H), 1.51 - 1.63 (m, 2H), 2.63 (t, J = 7.8 Hz, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 6.71 (d, J = 6.3 Hz, 1H), 7.09 (d, J = 8.5 Hz, 2H), 7.20 - 7.23 (m, 4H), 7.64 (s, 1H), 7.69 (d, J = 8.8 Hz, 2H), 8.15 (s, 1H), 8.52 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 474 (M⁺+1)

35 Example 258: 1-Ethylbutyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0361] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-hexanol (52 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (130 mg, yield 83%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.95 - 0.98 (m, 6H), 1.39 - 1.67 (m, 6H), 4.11 (s, 3H), 4.17 (s, 3H), 4.84 - 4.86 (m, 1H), 6.70 (d, J = 6.1 Hz, 1H), 6.77 (s, 1H), 7.18 (d, J = 9.0 Hz, 2H), 7.61 (d, J = 8.8 Hz, 2H), 7.64 (s, 1H), 8.13 (s, 1H), 8.53 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 426 (M⁺+1)

50 Example 259: 4-(Tert-butyl)phenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0362] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-(tert-butyl)phenol (77 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/

methanol to give the title compound (150 mg, yield 87%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.34 (s, 9H), 4.11 (s, 3H), 4.17 (s, 3H), 6.71 (d, J = 6.1 Hz, 1H), 7.13 (d, J = 8.8 Hz, 2H), 7.21 - 7.27 (m, 3H), 7.43 (d, J = 8.8 Hz, 2H), 7.64 (s, 1H), 7.68 (d, J = 8.8 Hz, 2H), 8.15 (s, 1H), 8.51 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 474 (M⁺+1)

Example 260: 2-Methoxyphenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0363] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (151 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-methoxyphenol (63 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (75 mg, yield 46%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.90 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 6.70 (brs, 1H), 6.85 (s, 1H), 6.92 - 7.02 (m, 4H), 7.15 - 7.25 (m, 3H), 7.64 (s, 1H), 7.70 (d, J = 8.3 Hz, 1H), 8.14 (s, 1H), 8.52 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 448 (M⁺+1)

Example 261: Hexyl N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0364] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-hexanol (48 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (106 mg, yield 72%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.92 (t, J = 7.1 Hz, 3H), 1.34 - 1.44 (m, 6H), 1.67 - 1.74 (m, 2H), 2.10 (s, 3H), 2.28 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.20 (t, J = 6.8 Hz, 2H), 6.45 (s, 1H), 6.56 (d, J = 6.6 Hz, 1H), 7.02 (d, J = 9.0 Hz, 1H), 7.67 (s, 1H), 7.75 (d, J = 9.3 Hz, 1H), 8.16 (s, 1H), 8.46 (t, J = 6.3 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 454 (M⁺+1)

Example 262: Hexyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0365] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-hexanol (48 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (154 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.92 (t, J = 7.1 Hz, 3H), 1.34 - 1.42 (m, 6H), 1.68 - 1.73 (m, 2H), 2.13 (s, 3H), 2.29 (s, 3H), 4.11 (s, 3H), 4.18 (s, 3H), 4.21 (t, J = 6.8 Hz, 2H), 6.42 (s, 1H), 6.59 (brs, 1H), 6.95 (s, 1H), 7.65 (s, 1H), 7.92 (s, 1H), 8.15 (s, 1H), 8.47 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 454 (M⁺+1)

Example 263: 1-Phenylpropyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0366] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-phenyl-1-propanol (35 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to

give the title compound (77 mg, yield 92%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.96 (t, J = 7.6 Hz, 3H), 1.88 - 1.93 (m, 1H), 1.99 - 2.05 (m, 1H), 4.10 (s, 3H), 4.16 (s, 3H), 5.69 (t, J = 7.3 Hz, 1H), 6.66 (d, J = 5.6 Hz, 1H), 6.84 (s, 1H), 7.16 (d, J = 8.8 Hz, 2H), 7.32 - 7.39 (m, 5H), 7.59 (d, J = 8.8 Hz, 2H), 7.63 (s, 1H), 8.15 (d, J = 4.1 Hz, 1H), 8.45 - 8.47 (m, 1H)

Mass spectrometry value (ESI-MS, m/z): 460 (M⁺+1)

Example 264: 1-Phenylpropyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0367] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-phenyl-1-propanol (31 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (76 mg, yield 97%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.97 (t, J = 7.5 Hz, 3H), 1.89 - 1.94 (m, 1H), 2.01 - 2.17 (m, 1H), 2.10 (s, 3H), 2.28 (s, 3H), 4.10 (s, 3H), 4.17 (s, 3H), 5.68 (t, J = 7.3 Hz, 1H), 6.50 (s, 1H), 6.55 (d, J = 6.3 Hz, 1H), 6.93 (s, 1H), 7.33 - 7.39 (m, 5H), 7.64 (s, 1H), 7.91 (s, 1H), 8.14 (s, 1H), 8.45 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 488 (M⁺+1)

Example 265: 1-Phenylpropyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0368] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-phenyl-1-propanol (31 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (52 mg, yield 66%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.96 (t, J = 7.3 Hz, 3H), 1.89 - 1.92 (m, 1H), 1.94 - 2.05 (m, 1H), 2.09 (s, 3H), 2.25 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.69 (t, J = 7.1 Hz, 1H), 6.52 (s, 1H), 6.54 (s, 1H), 6.99 (d, J = 8.5 Hz, 1H), 7.32 - 7.39 (m, 5H), 7.66 (s, 1H), 7.73 (brs, 1H), 8.15 (s, 1H), 8.45 (t, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 488 (M⁺+1)

Example 266: 4-Pentenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0369] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-penten-1-ol (22 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (77 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.80 - 1.83 (m, 2H), 2.16 - 2.20 (m, 2H), 4.10 (s, 3H), 4.17 (s, 3H), 4.23 (t, J = 6.6 Hz, 2H), 5.02 - 5.10 (m, 2H), 5.83 - 5.85 (m, 1H), 6.69 (d, J = 6.3 Hz, 1H), 6.76 (s, 1H), 7.18 (d, J = 8.8 Hz, 2H), 7.60 (d, J = 9.0 Hz, 2H), 7.64 (s, 1H), 8.15 (s, 1H), 8.48 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 410 (M⁺+1)

Example 267: 4-Pentenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0370] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-penten-1-ol (20 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform,

followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (71 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.81 - 1.85 (m, 2H), 2.13 (s, 3H), 2.18 - 2.20 (m, 2H), 2.29 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.23 (t, J = 6.6 Hz, 2H), 5.02 - 5.11 (m, 2H), 5.81 - 5.88 (m, 1H), 6.42 (s, 1H), 6.58 (d, J = 6.3 Hz, 1H), 6.95 (s, 1H), 7.64 (s, 1H), 7.91 (s, 1H), 8.16 (s, 1H), 8.46 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 438 (M⁺+1)

Example 268: 4-Pentenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0371] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-penten-1-ol (20 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (67 mg, yield 95%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.79 - 1.86 (m, 2H), 2.10 (s, 3H), 2.16 - 2.20 (m, 2H), 2.27 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 4.22 (t, J = 6.6 Hz, 2H), 5.02 - 5.10 (m, 2H), 5.81 - 5.88 (m, 1H), 6.44 (s, 1H), 6.56 (d, J = 6.6 Hz, 1H), 7.03 (d, J = 8.5 Hz, 1H), 7.67 (s, 1H), 7.76 (brs, 1H), 8.16 (d, J = 4.1 Hz, 1H), 8.45 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 438 (M⁺+1)

Example 269: 2,6-Dimethylphenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0372] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2,6-dimethylphenol (32 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (82 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.26 (s, 6H), 4.11 (s, 3H), 4.17 (s, 3H), 6.70 (d, J = 7.6 Hz, 1H), 7.10 (s, 2H), 7.22 - 7.26 (m, 4H), 7.65 (s, 1H), 7.71 (d, J = 8.5 Hz, 2H), 8.16 (d, J = 4.1 Hz, 1H), 8.48 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 446 (M⁺+1)

Example 270: 2,6-Dimethylphenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0373] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2,6-dimethylphenol (28 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (76 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.13 (s, 3H), 2.28 (s, 6H), 2.39 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 6.59 (d, J = 5.9 Hz, 1H), 7.01 (s, 1H), 7.11 (s, 2H), 7.25 - 7.27 (m, 2H), 7.65 (s, 1H), 7.98 (brs, 1H), 8.16 (s, 1H), 8.47 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 474 (M⁺+1)

Example 271: 2,6-Dimethylphenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0374] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2,6-dimethylphenol (28 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (76 mg, yield 100%).

roform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (68 mg, yield 89%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.14 (s, 3H), 2.28 (s, 6H), 2.38 (s, 3H), 4.12 (s, 3H), 4.18 (s, 3H), 6.56 (d, J = 6.8 Hz, 1H), 7.00 - 7.10 (m, 4H), 7.25 - 7.27 (m, 1H), 7.67 (s, 1H), 8.16 (s, 1H), 8.46 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 474 (M⁺+1)

Example 272: 4-Butylphenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0375] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-butylphenol (35 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (12 mg, yield 15%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.90 - 0.96 (m, 3H), 1.33 - 1.44 (m, 2H), 1.50 - 1.65 (m, 2H), 2.13 (s, 3H), 2.28 (s, 3H), 2.53 (t, J = 7.8 Hz, 1H), 2.63 (t, J = 8.1 Hz, 1H), 4.11 (s, 3H), 4.17 (s, 3H), 6.44 (s, 1H), 6.58 (d, J = 6.3 Hz, 1H), 6.75 (d, J = 8.5 Hz, 1H), 6.95 (s, 1H), 7.02 (t, J = 8.5 Hz, 1H), 7.11 (d, J = 8.5 Hz, 1H), 7.22 (d, J = 8.8 Hz, 1H), 7.64 (s, 1H), 7.89 (brs, 1H), 8.16 (s, 1H), 8.45 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 502 (M⁺+1)

Example 273: 4-Butylphenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0376] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-butylphenol (35 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (44 mg, yield 55%).

¹H-NMR (CDCl₃-d₁, 400 MHz) : δ 0.94 (t, J = 7.3 Hz, 3H), 1.34 - 1.44 (m, 2H), 1.56 - 1.63 (m, 2H), 2.13 (s, 3H), 2.36 (s, 3H), 2.63 (t, J = 7.8 Hz, 2H), 4.12 (s, 3H), 4.17 (s, 3H), 6.57 (d, J = 10.7 Hz, 1H), 7.04 - 7.26 (m, 6H), 7.67 (s, 1H), 7.84 (brs, 1H), 8.17 (d, J = 4.4 Hz, 1H), 8.46 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

Example 274: 4-(Tert-butyl)phenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0377] 4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-(tert-butyl)phenol (35 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (35 mg, yield 44%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.54 (s, 9H), 2.13 (s, 3H), 2.37 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 6.59 (s, 1H), 6.77 (d, J = 8.8 Hz, 1H), 6.95 (s, 1H), 7.00 (s, 1H), 7.14 (d, J = 8.8 Hz, 2H), 7.43 (d, J = 8.8 Hz, 2H), 7.65 (s, 1H), 7.99 (brs, 1H), 8.16 (s, 1H), 8.46 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 502 (M⁺+1)

Example 275: 4-(Tert-butyl)phenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0378] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-(tert-butyl)phenol (35

mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (34 mg, yield 42%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.54 (s, 9H), 2.13 (s, 3H), 2.36 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 6.57 (d, J = 5.6 Hz, 1H), 6.77 (d, J = 8.8 Hz, 1H), 7.05 (d, J = 9.3 Hz, 1H), 7.14 (d, J = 8.8 Hz, 2H), 7.42 (d, J = 8.8 Hz, 2H), 7.67 (s, 1H), 7.84 (brs, 1H), 8.17 (d, J = 3.9 Hz, 1H), 8.45 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

Example 276: 1-Ethylbutyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0379] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-hexanol (24 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (20 mg, yield 27%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.95 - 0.99 (m, 6H), 1.40 - 1.65 (m, 6H), 2.13 (s, 3H), 2.29 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.85 (brs, 1H), 6.41 (s, 1H), 6.57 (d, J = 4.6 Hz, 1H), 6.94 (s, 1H), 7.65 (s, 1H), 7.96 (s, 1H), 8.15 (s, 1H), 8.45 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 454 (M⁺+1)

Example 277: 1-Ethylbutyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0380] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-hexanol (24 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (39 mg, yield 53%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.94 - 0.99 (m, 6H), 1.40 - 1.68 (m, 6H), 2.10 (s, 3H), 2.28 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 4.85 (brs, 1H), 6.55 (d, J = 5.9 Hz, 1H), 7.00 - 7.03 (m, 1H), 7.79 (s, 1H), 8.16 - 8.17 (m, 1H), 8.44 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 454 (M⁺+1)

Example 278: 2-Methoxyphenyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0381] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-methoxyphenol (29 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (39 mg, yield 51%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.12 (s, 3H), 2.38 (s, 3H), 3.90 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 6.60 (d, J = 5.9 Hz, 1H), 6.86 - 7.04 (m, 4H), 7.17 - 7.19 (m, 1H), 7.65 (s, 1H), 7.99 (s, 1H), 8.16 (d, J = 4.1 Hz, 1H), 8.47 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 476 (M⁺+1)

Example 279: 2-Methoxyphenyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0382] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-methoxyphenol (29 mg)

was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (31 mg, yield 41%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.13 (s, 3H), 2.37 (s, 3H), 3.89 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 6.57 (brs, 1H), 6.86 - 7.06 (m, 5H), 7.18 (d, J = 6.3 Hz, 1H), 7.67 (d, J = 2.0 Hz, 1H), 8.17 (d, J = 3.9 Hz, 1H), 8.46 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 476 (M⁺+1)

Example 280: 2,6-Dimethoxyphenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0383] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2,6-dimethoxyphenol (40 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (80 mg, yield 92%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.87 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 6.60 - 6.67 (m, 4H), 7.17 - 7.21 (m, 2H), 7.64 (s, 1H), 7.70 (d, J = 8.8 Hz, 2H), 8.15 (s, 1H), 8.49 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 478 (M⁺+1)

Example 281: 2,6-Dimethoxyphenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0384] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2,6-dimethoxyphenol (35 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (75 mg, yield 93%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.33 (s, 3H), 2.38 (s, 3H), 3.89 (s, 6H), 4.11 (s, 3H), 4.17 (s, 3H), 6.60 (brs, 1H), 6.67 (d, J = 8.5 Hz, 1H), 6.98 - 7.19 (m, 2H), 7.65 (s, 1H), 8.04 (s, 1H), 8.15 (s, 1H), 8.48 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 506 (M⁺+1)

Example 282: 2,6-Dimethoxyphenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0385] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2,6-dimethoxyphenol (35 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (74 mg, yield 91%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.21 (s, 3H), 2.37 (s, 3H), 3.88 (s, 3H), 3.89 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 6.58 - 6.60 (m, 2H), 6.66 (d, J = 8.5 Hz, 1H), 6.78 - 6.82 (m, 1H), 7.02 - 7.05 (m, 1H), 7.16 - 7.20 (m, 1H), 7.67 (s, 1H), 7.87 (s, 1H), 8.16 (s, 1H), 8.47 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 506 (M⁺+1)

Example 283: Cyclohexylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0386] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclohexylmethanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate

solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (49 mg, yield 61%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.03 - 1.04 (m, 2H), 1.21-1.27 (m, 4H), 1.78 - 1.80 (m, 5H), 4.02 (d, J = 6.3 Hz, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 6.70 (d, J = 5.9 Hz, 1H), 6.88 (s, 1H), 7.18 (d, J = 8.8 Hz, 2H), 7.61 (d, J = 8.5 Hz, 2H), 7.64 (s, 1H), 8.15 (d, J = 4.1 Hz, 1H), 8.47 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 438 (M⁺+1)

Example 284: Cyclohexylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0387] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclohexylmethanol (26 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (62 mg, yield 83%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.02 - 1.04 (m, 2H), 1.21 - 1.31 (m, 4H), 1.72 - 1.79 (m, 5H), 2.13 (s, 3H), 2.29 (s, 3H), 4.03 (d, J = 6.3 Hz, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 6.42 (s, 1H), 6.58 (d, J = 4.9 Hz, 1H), 6.95 (s, 1H), 7.65 (s, 1H), 7.93 (s, 1H), 8.16 (d, J = 4.1 Hz, 1H), 8.46 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 466 (M⁺+1)

Example 285: Cyclohexylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0388] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclohexylmethanol (26 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (48 mg, yield 64%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.97 - 1.07 (m, 2H), 1.17 - 1.32 (m, 4H), 1.69 - 1.82 (m, 5H), 2.10 (s, 3H), 2.28 (s, 3H), 4.02 (d, J = 6.6 Hz, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 6.44 (s, 1H), 6.55 (d, J = 5.4 Hz, 1H), 7.00 - 7.04 (m, 2H), 7.67 (s, 1H), 7.77 (brs, 1H), 8.16 (d, J = 4.1 Hz, 1H), 8.44 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 466 (M⁺+1)

Example 286: Cycloheptyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0389] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cycloheptanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (68 mg, yield 85%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.47 - 1.79 (m, 12H), 4.10 (s, 3H), 4.17 (s, 3H), 4.90 - 4.96 (m, 1H), 6.70 (d, J = 5.9 Hz, 1H), 6.83 (s, 1H), 7.17 (d, J = 9.0 Hz, 2H), 7.60 (d, J = 8.5 Hz, 2H), 7.64 (s, 1H), 8.15 (s, 1H), 8.47 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 438 (M⁺+1)

Example 287: Cycloheptyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0390] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cycloheptanol (26 mg)

was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (68 mg, yield 91%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.51 - 1.74 (m, 12H), 2.13 (s, 3H), 2.29 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.96 (brs, 1H), 6.40 (s, 1H), 6.58 (d, J = 6.3 Hz, 1H), 6.94 (s, 1H), 7.65 (s, 1H), 7.95 (s, 1H), 8.16 (d, J = 4.1 Hz, 1H), 8.46 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 466 (M⁺+1)

Example 288: Cycloheptyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0391] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cycloheptanol (26 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (66 mg, yield 88%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.51 - 1.74 (m, 12H), 2.10 (s, 3H), 2.27 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 4.96 (brs, 1H), 6.43 (s, 1H), 6.56 (d, J = 6.6 Hz, 1H), 7.02 (d, J = 9.3 Hz, 1H), 7.67 (s, 1H), 7.78 (s, 1H), 8.16 (d, J = 3.9 Hz, 1H), 8.45 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 466 (M⁺+1)

Example 289: 2-Methylphenyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0392] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, o-cresol (25 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (62 mg, yield 84%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.13 (s, 3H), 2.31 (s, 3H), 2.39 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 6.60 (d, J = 6.3 Hz, 1H), 6.85 (s, 1H), 7.00 (s, 1H), 7.14 - 7.27 (m, 4H), 7.65 (s, 1H), 7.98 (brs, 1H), 8.15 (d, J = 3.7 Hz, 1H), 8.52 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 460 (M⁺+1)

Example 290: 3-Methoxyphenyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0393] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-methoxyphenol (29 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (30 mg, yield 39%).

¹H-NMR (CDCl₃-d₁, 400 MHz) : δ 2.14 (s, 3H), 2.37 (s, 3H), 3.83 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 6.42 (s, 1H), 6.59 (brs, 1H), 6.79 - 6.84 (m, 3H), 7.00 (s, 1H), 7.30 - 7.34 (m, 1H), 7.65 (s, 1H), 7.98 (brs, 1H), 8.16 (s, 1H), 8.49 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 476 (M⁺+1)

Example 291: 3-Methoxyphenyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0394] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine

(0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-methoxyphenol (29 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (23 mg, yield 30%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.13 (s, 3H), 2.36 (s, 3H), 3.83 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 6.44 - 6.48 (m, 1H), 6.56 - 6.58 (m, 1H), 6.78 - 6.83 (m, 3H), 7.06 (d, J = 8.8 Hz, 1H), 7.29 - 7.33 (m, 1H), 7.67 (s, 1H), 7.81 (brs, 1H), 8.16 (d, J = 3.4 Hz, 1H), 8.50 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 476 (M⁺⁺¹)

Example 292: 1,2,3,4-Tetrahydro-2-naphthalenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0395] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1,2,3,4-tetrahydro-2-naphthalenol (34 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (80 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.08 - 2.13 (m, 2H), 2.12 (s, 3H), 2.27 (s, 3H), 2.80 - 3.24 (m, 4H), 4.11 (s, 3H), 4.17 (s, 3H), 5.30 (brs, 1H), 6.43 (s, 1H), 6.57 (d, J = 6.6 Hz, 1H), 6.94 (s, 1H), 7.11 - 7.18 (m, 4H), 7.64 (s, 1H), 7.94 (brs, 1H), 8.15 (d, J = 3.9 Hz, 1H), 8.48 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 500 (M⁺⁺¹)

Example 293: 1,2,3,4-Tetrahydro-2-naphthalenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0396] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1,2,3,4-tetrahydro-2-naphthalenol (34 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (55 mg, yield 69%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.08 - 2.13 (m, 2H), 2.09 (s, 3H), 2.25 (s, 3H), 2.92 - 3.23 (m, 4H), 4.11 (s, 3H), 4.17 (s, 3H), 5.29 (brs, 1H), 6.46 (s, 1H), 6.55 (d, J = 6.1 Hz, 1H), 7.01 (d, J = 8.8 Hz, 1H), 7.12 - 7.18 (m, 4H), 7.67 (s, 1H), 7.77 (brs, 1H), 8.16 (d, J = 3.7 Hz, 1H), 8.48 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 500 (M⁺⁺¹)

Example 294: 4-Phenylphenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0397] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-phenylphenol (44 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (29 mg, yield 32%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 4.11 (s, 3H), 4.17 (s, 3H), 6.71 (s, 1H), 6.93 (d, J = 8.5 Hz, 1H), 7.26 - 7.78 (m, 13H), 8.14 (brs, 1H), 8.53 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 494 (M⁺⁺¹)

Example 295: 4-Phenylphenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0398] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-phenylphenol (39 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (55 mg, yield 66%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.14 (s, 3H), 2.28 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 6.44 (s, 1H), 6.60 (brs, 1H), 6.95 (s, 1H), 7.01 (brs, 1H), 7.26 - 7.52 (m, 4H), 7.57 - 7.65 (m, 5H), 7.89 (s, 1H), 8.15 (brs, 1H), 8.48 (brs, 1H)
Mass spectrometry value (ESI-MS, m/z): 522 (M⁺+1)

Example 296: 4-Phenylphenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0399] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-phenylphenol (39 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (36 mg, yield 43%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.14 (s, 3H), 2.38 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 6.57 - 6.59 (m, 1H), 6.92 - 7.08 (m, 2H), 7.25 - 7.79 (m, 10H), 8.16 - 8.17 (m, 1H), 8.47 - 8.52 (m, 1H)
Mass spectrometry value (ESI-MS, m/z): 522 (M⁺+1)

Example 297: Phenethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0400] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-phenyl-1-ethanol (32 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (42 mg, yield 51%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.03 (t, J = 6.8 Hz, 2H), 4.10 (s, 3H), 4.17 (s, 3H), 4.45 (t, J = 7.1 Hz, 2H), 6.69 (s, 1H), 6.78 (s, 1H), 7.16 - 7.36 (m, 7H), 7.52 - 7.64 (m, 3H), 8.15 (s, 1H), 8.49 (brs, 1H)
Mass spectrometry value (ESI-MS, m/z): 446 (M⁺+1)

Example 298: Phenethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0401] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-phenyl-1-ethanol (28 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (76 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.12 (s, 3H), 2.26 (s, 3H), 3.04 (t, J = 6.8 Hz, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 4.44 (t, J = 7.1 Hz, 2H), 6.40 (s, 1H), 6.59 (s, 1H), 6.95 (s, 1H), 7.26 - 7.36 (m, 5H), 7.64 (s, 1H), 7.86 (brs, 1H), 8.16 (s, 1H), 8.47 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 474 (M⁺+1)

Example 299: Phenethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0402] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-phenyl-1-ethanol (28 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (60 mg, yield 79%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.09 (s, 3H), 2.24 (s, 3H), 3.03 (t, J = 6.8 Hz, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 4.44 (t, J = 7.1 Hz, 2H), 6.42 (s, 1H), 6.55 (d, J = 5.9 Hz, 1H), 7.01 (d, J = 8.5 Hz, 1H), 7.26 - 7.36 (m, 5H), 7.66 (s, 1H), 8.16 (d, J = 4.1 Hz, 1H), 8.46 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 474 (M⁺+1)

Example 300: 2-(Tert-butyl)phenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0403] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-(tert-butyl)phenol (39 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (64 mg, yield 74%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.42 (s, 9H), 4.11 (s, 3H), 4.17 (s, 3H), 6.72 (brs, 1H), 7.11 (d, J = 6.3 Hz, 1H), 7.22 - 7.26 (m, 6H), 7.43 - 7.45 (m, 1H), 7.65 (s, 1H), 7.71 (brs, 1H), 8.15 (brs, 1H), 8.51 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 474 (M⁺+1)

Example 301: 2-(Tert-butyl)phenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0404] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-(tert-butyl)phenol (35 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (77 mg, yield 96%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.56 (s, 9H), 2.13 (s, 3H), 2.39 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 6.59 (brs, 1H), 7.01 (s, 1H), 7.13 (d, J = 7.8 Hz, 1H), 7.21 - 7.26 (m, 3H), 7.43 - 7.45 (m, 1H), 7.65 (s, 1H), 8.15 (s, 1H), 8.49 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

Example 302: 2-(Tert-butyl)phenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0405] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-(tert-butyl)phenol (35 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (48 mg, yield 60%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.56 (s, 9H), 2.14 (s, 3H), 2.38 (s, 3H), 4.12 (s, 3H), 4.18 (s, 3H), 6.55 (brs, 1H), 7.06 (d, J = 9.0 Hz, 1H), 7.14 (d, J = 7.8 Hz, 1H), 7.21 - 7.26 (m, 4H), 7.42 (brs, 1H), 7.67 (s, 1H), 8.16 (s, 1H), 8.48 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

Example 303: 2-Piperidinoethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0406] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-piperidino-1-ethanol (34 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (66 mg, yield 74%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.89 - 1.93 (m, 4H), 2.29 - 2.45 (m, 2H), 2.74 - 2.86 (m, 2H), 3.36 (brs, 1H), 3.70 - 3.73 (m, 2H), 4.10 (s, 3H), 4.16 (s, 3H), 4.56 - 4.58 (m, 2H), 6.72 (d, J = 6.3 Hz, 1H), 7.15 (d, J = 8.8 Hz, 2H), 7.65 (s, 1H) 7.74 (d, J = 8.8 Hz, 2H), 8.10 (s, 1H), 8.52 (t, J = 6.3 Hz, 1H), 9.60 (brs, 1H), 11.42 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 453 (M⁺+1)

Example 304: 2-Piperidinoethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0407] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-piperidino-1-ethanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (42 mg, yield 51%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.50 (brs, 2H), 1.85 (brs, 2H), 2.11 (s, 3H), 2.43 (brs, 5H), 2.78 (brs, 2H), 3.34 (brs, 2H), 3.70 (brs, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 4.56 (brs, 2H), 6.61 (brs, 1H), 6.95 (s, 1H), 7.66 (s, 1H), 7.86 (s, 1H), 8.13 (s, 1H), 8.48 (brs, 1H), 11.85 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 481 (M⁺+1)

Example 305: 2-Piperidinoethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0408] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-piperidino-1-ethanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (83 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.88 (brs, 2H), 2.09 (s, 3H), 2.31 - 2.39 (m, 1H), 2.39 (s, 3H), 2.47 - 2.51 (m, 1H), 2.71 - 2.80 (m, 2H), 3.12 - 3.14 (m, 1H), 3.33 (brs, 2H), 3.69 (brs, 2H), 4.01 - 4.03 (m, 1H), 4.12 (s, 3H), 4.17 (s, 3H), 4.54 - 4.55 (m, 2H), 6.58 (d, J = 6.3 Hz, 1H), 6.98 (d, J = 8.8 Hz, 1H), 7.68 (s, 1H), 7.76 (d, J = 9.0 Hz, 1H), 8.14 (s, 1H), 8.48 - 8.49 (m, 1H), 11.83 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 481 (M⁺+1)

Example 306: 2-Morpholinoethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0409] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-morpholino-1-ethanol (34 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (43 mg, yield 48%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.11 (brs, 2H), 3.42 (brs, 2H), 3.66 (brs, 2H), 4.01 - 4.19 (m, 2H), 4.10 (s, 3H), 4.16 (s, 3H), 4.46 (brs, 2H), 4.62 (brs, 2H), 6.73 (s, 1H), 7.14 (s, 1H), 7.65 (s, 1H), 7.73 (s, 2H), 8.09 (s, 1H), 8.54 (brs,

1H), 9.45 (s, 1H), 12.38 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 455 (M⁺+1)

Example 307: 2-Morpholinoethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0410] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-morpholino-1-ethanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (63 mg, yield 76%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.11 (s, 3H), 2.42 (s, 3H), 3.06 (brs, 2H), 3.41 (brs, 2H), 3.62 (brs, 2H), 4.02 - 4.17 (m, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 4.52 - 4.59 (m, 4H), 6.60 (brs, 1H), 6.95 (s, 1H), 7.66 (s, 1H), 7.85 (s, 1H), 8.13 (s, 2H), 8.30 (brs, 1H), 8.50 (brs, 1H), 12.79 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 483 (M⁺+1)

Example 308: 2-Morpholinoethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0411] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-morpholino-1-ethanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (74 mg, yield 89%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.09 (s, 3H), 2.39 (s, 3H), 3.03 (brs, 2H), 3.38 (brs, 2H), 3.62 (d, J = 11.7 Hz, 2H), 4.02 - 4.04 (m, 2H), 4.12 (s, 3H), 4.17 (s, 3H), 4.50 - 4.59 (m, 4H), 6.57 (d, J = 6.3 Hz, 1H), 6.99 (d, J = 8.8 Hz, 1H), 7.67 (s, 1H), 7.77 (d, J = 9.3 Hz, 1H), 8.14 (s, 1H), 8.32 (brs, 1H), 8.48 (s, 1H), 12.87 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 483 (M⁺+1)

Example 309: 6-(Dimethylamino)hexyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0412] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 6-(dimethylamino)-1-hexanol (38 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (31 mg, yield 34%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.43 - 1.87 (m, 8H), 2.82 - 3.08 (m, 8H), 4.11 (s, 3H), 4.16 (s, 3H), 4.11 - 4.22 (m, 2H), 6.72 (s, 1H), 7.14 (s, 2H), 7.65 (s, 1H), 7.87 (s, 2H), 8.11 (s, 1H), 8.50 (brs, 1H), 8.80 (brs, 1H), 12.00 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 469 (M⁺+1)

Example 310: 6-(Dimethylamino)hexyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0413] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 6-(dimethylamino)-1-hexanol (33 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (48 mg, yield 56%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.53 - 1.93 (m, 8H), 2.13 (s, 3H), 2.33 (s, 3H), 2.83 (s, 6H), 3.02 (brs, 2H), 4.11

(s, 3H), 4.17 (s, 3H), 4.11 - 4.21 (m, 2H), 6.61 (brs, 1H), 6.95 (s, 1H), 7.65 (s, 1H), 7.85 (s, 1H), 8.14 (s, 1H), 8.49 (brs, 1H), 12.39 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 497 (M⁺+1)

5 Example 311: 6-(Dimethylamino)hexyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0414] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 6-(dimethylamino)-1-hex-
10 anol (33 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (66 mg, yield 77%).

15 ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.75 - 2.01 (m, 8H), 2.10 (s, 3H), 2.31 (s, 3H), 2.83 (s, 6H), 3.03 (s, 2H), 4.12 (s, 3H), 4.17 (s, 3H), 4.12 - 4.21 (m, 2H), 6.59 (s, 1H), 7.01 (d, J = 8.1 Hz, 1H), 7.68 (s, 1H), 8.13 (s, 1H), 8.50 (brs, 1H), 12.02 (brs, 1H), 12.30 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 497 (M⁺+1)

20 Example 312: Cyclohexyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0415] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cyclohexanol (26 mg) was added
25 thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (60 mg, yield 71%).

30 ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.21 - 1.57 (m, 6H), 1.76 (brs, 2H), 1.94 (brs, 2H), 4.12 (s, 3H), 4.19 (s, 3H), 4.78 (brs, 1H), 6.72 (s, 1H), 7.19 (d, J = 9.0 Hz, 2H), 7.57 (d, J = 8.8 Hz, 2H), 7.62 (s, 1H), 8.15 (s, 1H), 8.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 425 (M⁺+1)

35 Example 313: Cyclohexyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0416] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cyclohexanol (23 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium
40 bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (61 mg, yield 77%).

45 ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.30 - 1.58 (m, 6H), 1.78 (brs, 2H), 1.95 (brs, 2H), 4.12 (s, 3H), 4.20 (s, 3H), 4.79 (brs, 1H), 7.16 - 7.20 (m, 2H), 7.32 (s, 1H), 7.59 (s, 1H), 8.17 (s, 1H), 8.40 (d, J = 9.3 Hz, 1H), 8.82 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 459 (M⁺+1)

Example 314: Propyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0417] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-propanol (16 mg) was added
50 thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (77 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.00 (t, J = 7.3 Hz, 3H), 1.68 - 1.75 (m, 2H), 4.12 (s, 3H), 4.16 (t, J = 6.8 Hz,

2H), 4.19 (s, 3H), 6.77 (s, 1H), 7.20 (d, J = 9.0 Hz, 2H), 7.58 (d, J = 8.8 Hz, 2H), 7.62 (s, 1H), 8.15 (s, 1H), 8.81 (s, 1H)
Mass spectrometry value (ESI-MS, m/z): 384 (M⁺+1)

Example 315: 2-Methoxybenzyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0418] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-methoxyphenyl)methanol (36 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (91 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.88 (s, 3H), 4.12 (s, 3H), 4.19 (s, 3H), 5.29 (s, 2H), 6.84 (s, 1H), 6.92 - 7.00 (m, 2H), 7.19 (d, J = 9.0 Hz, 2H), 7.33 - 7.40 (m, 2H), 7.57 (d, J = 9.0 Hz, 2H), 7.62 (s, 1H), 8.15 (s, 1H), 8.80 (s, 1H)
Mass spectrometry value (ESI-MS, m/z) : 463 (M⁺+1)

Example 316: 2-Methoxybenzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0419] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-methoxyphenyl)methanol (32 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (79 mg, yield 93%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.89 (s, 3H), 4.12 (s, 3H), 4.20 (s, 3H), 5.32 (s, 2H), 6.89 (s, 2H), 6.89 - 7.01 (m, 3H), 7.18 - 7.21 (m, 1H), 7.29 - 7.43 (m, 3H), 7.59 (s, 1H), 8.16 (s, 1H), 8.43 (d, J = 9.0 Hz, 1H), 8.83 (s, 1H), 9.57 (brs, 1H)
Mass spectrometry value (ESI-MS, m/z): 497 (M⁺+1)

Example 317: 2-Chlorobenzyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0420] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77, mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-chlorophenyl)methanol (37 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (92 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 4.12 (s, 3H), 4.19 (s, 3H), 5.35 (s, 2H), 7.20 (d, J = 9.0 Hz, 2H), 7.29 - 7.32 (m, 2H), 7.42 - 7.44 (m, 1H), 7.48 - 7.52 (m, 1H), 7.59 (d, J = 8.8 Hz, 2H), 7.62 (s, 1H), 8.15 (s, 1H), 8.79 (s, 1H)
Mass spectrometry value (ESI-MS, m/z): 467 (M⁺+1)

Example 318: 2-Chlorobenzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0421] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-chlorophenyl)methanol (33 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (80 mg, yield 93%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 4.12 (s, 3H), 4.20 (s, 3H), 5.38 (s, 2H), 7.19 - 7.22 (m, 1H), 7.30 - 7.35 (m, 3H), 7.43 - 7.45 (m, 1H), 7.49 - 7.51 (m, 1H), 7.59 (s, 1H), 8.16 (s, 1H), 8.41 (d, J = 9.0 Hz, 1H), 8.82 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 501 (M⁺+1)

Example 319: 2-Methylbenzyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0422] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-methylphenyl)methanol (32 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (79 mg, yield 90%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.41 (s, 3H), 4.12 (s, 3H), 4.19 (s, 3H), 5.26 (s, 2H), 6.87 (s, 1H), 7.20 (d, J = 9.0 Hz, 2H), 7.22 - 7.30 (m, 3H), 7.37 - 7.39 (m, 1H), 7.58 (d, J = 8.8 Hz, 2H), 7.61 (s, 1H), 8.15 (s, 1H), 8.79 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 447 (M⁺+1)

Example 320: 2-Methylbenzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0423] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-methylphenyl)methanol (28 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (62 mg, yield 75%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.43 (s, 3H), 4.12 (s, 3H), 4.20 (s, 3H), 5.28 (s, 2H), 7.18 - 7.33 (m, 5H), 7.40 (d, J = 6.8 Hz, 1H), 7.59 (s, 1H), 8.16 (s, 1H), 8.41 (d, J = 9.0 Hz, 1H), 8.82 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 481 (M⁺+1)

Example 321: Butyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0424] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-butanol (19 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (34 mg, yield 46%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.97 (t, J = 7.3 Hz, 3H), 1.41 - 1.49 (m, 2H), 1.62 - 1.72 (m, 2H), 4.10 (s, 3H), 4.17 (s, 3H), 4.21 (t, J = 6.8 Hz, 2H), 6.70 (d, J = 6.3 Hz, 1H), 6.85 (s, 1H), 7.18 (d, J = 8.8 Hz, 2H), 7.61 (d, J = 8.8 Hz, 2H), 7.64 (s, 1H), 8.15 (s, 1H), 8.47 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 397 (M⁺+1)

Example 322: Butyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0425] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-butanol (17 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (65 mg, yield 94%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.99 (t, J = 7.3 Hz, 3H), 1.41 - 1.50 (m, 2H), 1.67 - 1.74 (m, 2H), 2.13 (s, 3H), 2.29 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.22 (t, J = 6.8 Hz, 2H), 6.42 (s, 1H), 6.59 (brs, 1H), 6.95 (s, 1H), 7.65 (s, 1H), 7.92 (s, 1H), 8.16 (s, 1H), 8.46 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 426 (M⁺+1)

Example 323: Butyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0426] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-butanol (17 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (60 mg, yield- 87%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.98 (t, J = 7.3 Hz, 3H), 1.40 - 1.49 (m, 2H), 1.67 - 1.73 (m, 2H), 2.10 (s, 3H), 2.28 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 4.21 (t, J = 6.8 Hz, 2H), 6.46 (s, 1H), 6.56 (d, J = 6.3 Hz, 1H), 7.02 (d, J = 8.8 Hz, 1H), 7.67 (s, 1H), 7.76 (d, J = 8.5 Hz, 1H), 8.15 (s, 1H), 8.47 (t, J = 6.3 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 426 (M⁺+1)

Example 324: Isopropyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0427] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-propanol (16 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (42 mg, yield 59%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.33 (d, J = 6.3 Hz, 6H), 4.11 (s, 3H), 4.17 (s, 3H), 5.02 - 5.09 (m, 1H), 6.70 (d, J = 6.1 Hz, 1H), 6.74 (s, 1H), 7.18 (d, J = 9.0 Hz, 1H), 7.60 (d, J = 8.8 Hz, 2H), 7.64 (s, 1H), 8.15 (s, 1H), 8.47 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 383 (M⁺+1)

Example 325: Isopropyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0428] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-propanol (14 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (50 mg, yield 75%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.34 (d, J = 6.3 Hz, 6H), 2.13 (s, 3H), 2.29 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.04 - 5.07 (m, 1H), 6.38 (s, 1H), 6.58 (brs, 1H), 6.95 (s, 1H), 7.65 (s, 1H), 7.95 (s, 1H), 8.15 (s, 1H), 8.46 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 412 (M⁺+1)

Example 326: Octadecyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0429] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-octadecanol (70 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (54 mg, yield 51%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.88 (t, J = 7.1 Hz, 3H), 1.20 - 1.45 (m, 30H), 1.68 - 1.72 (m, 2H), 4.10 (s, 3H), 4.17 (s, 3H), 4.20 (t, J = 6.6 Hz, 2H), 6.69 (d, J = 6.3 Hz, 1H), 6.77 (s, 1H), 7.18 (d, J = 8.8 Hz, 2H), 7.60 (d, J = 8.8 Hz, 2H), 7.64 (s, 1H), 8.15 (s, 1H), 8.47 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 594 ($M^{+}+1$)

Example 327: Octadecyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0430] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-octadecanol (62 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (83 mg, yield 84%).

$^1\text{H-NMR}$ ($\text{CDCl}_3\text{-d}_1$, 400 MHz): δ 0.88 (t, $J = 7.1$ Hz, 3H), 1.26 - 1.42 (m, 30H), 1.67 - 1.73 (m, 2H), 2.13 (s, 3H), 2.29 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.20 (t, $J = 6.6$ Hz, 2H), 6.42 (s, 1H), 6.59 (brs, 1H), 6.95 (s, 1H), 7.65 (s, 1H), 7.92 (s, 1H), 8.15 (s, 1H), 8.47 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 622 ($M^{+}+1$)

Example 328: Octadecyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0431] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-octadecanol (62 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (96 mg, yield 97%).

$^1\text{H-NMR}$ ($\text{CDCl}_3\text{-d}_1$, 400 MHz) : δ 0.88 (t, $J = 6.8$ Hz, 3H), 1.21 - 1.42 (m, 30H), 1.67 - 1.72 (m, 2H), 2.10 (s, 3H), 2.27 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.20 (t, $J = 6.8$ Hz, 2H), 6.44 (s, 1H), 6.56 (d, $J = 6.6$ Hz, 1H), 7.02 (d, $J = 8.5$ Hz, 1H), 7.67 (s, 1H), 7.75 (brs, 1H), 8.15 (s, 1H), 8.47 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 622 ($M^{+}+1$)

Example 329: 1-Ethylpentyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0432] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-heptanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (46 mg, yield 57%).

$^1\text{H-NMR}$ ($\text{CDCl}_3\text{-d}_1$, 400 MHz): δ 0.90 - 0.98 (m, 6H), 1.35 - 1.36 (m, 4H), 1.62 - 1.69 (m, 4H), 4.11 (s, 3H), 4.17 (s, 3H), 4.80 - 4.86 (m, 1H), 6.69 (d, $J = 6.3$ Hz, 1H), 6.79 (s, 1H), 7.18 (d, $J = 8.8$ Hz, 2H), 7.62 (d, $J = 9.0$ Hz, 2H), 7.64 (s, 1H), 8.15 (s, 1H), 8.47 (t, $J = 6.6$ Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 440 ($M^{+}+1$)

Example 330: 1-Ethylpentyl N-{4-[(6,7-dimethoxy-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0433] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-heptanol (27 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (59 mg, yield 78%).

$^1\text{H-NMR}$ ($\text{CDCl}_3\text{-d}_1$, 400 MHz): δ 0.93 - 0.99 (m, 6H), 1.30 - 1.45 (m, 4H), 1.57 - 1.68 (m, 4H), 2.13 (s, 3H), 2.30

(s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.82 - 4.85 (m, 1H), 6.42 (s, 1H), 6.58 (d, J = 6.3 Hz, 1H), 6.95 (s, 1H), 7.65 (s, 1H), 7.96 (s, 1H), 8.15 (s, 1H), 8.46 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 468 (M⁺+1)

5 Example 331: 1-Ethylpentyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0434] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-heptanol (27 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (46 mg, yield 61%).

15 ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.91 - 0.99 (m, 6H), 1.30 - 1.45 (m, 4H), 1.59 - 1.68 (m, 4H), 2.10 (s, 3H), 2.28 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 4.82 - 4.84 (m, 1H), 6.43 (s, 1H), 6.55 (d, J = 6.6 Hz, 1H), 7.02 (d, J = 8.8 Hz, 1H), 7.67 (s, 1H), 7.78 (brs, 1H), 8.15 (s, 1H), 8.47 (t, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 468 (M⁺+1)

20 Example 332: 1-Propylbutyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]carbamate

[0435] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-heptanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (48 mg, yield 60%).

30 ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.95 (t, J = 7.3 Hz, 6H), 1.37 - 1.45 (m, 4H), 1.53 - 1.63 (m, 4H), 4.11 (s, 3H), 4.17 (s, 3H), 4.89 - 4.94 (m, 1H), 6.69 (d, J = 6.6 Hz, 1H), 6.76 (s, 1H), 7.18 (d, J = 8.8 Hz, 2H), 7.61 (d, J = 8.8 Hz, 2H), 7.64 (s, 1H), 8.15 (s, 1H), 8.47 (t, J = 6.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 440 (M⁺+1)

35 Example 333: 1-Propylbutyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0436] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-heptanol (27 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (57 mg, yield 76%).

45 ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.96 (t, J = 7.3 Hz, 6H), 1.38 - 1.46 (m, 4H), 1.54 - 1.64 (m, 4H), 2.13 (s, 3H), 2.29 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.91 - 4.94 (m, 1H), 6.41 (s, 1H), 6.57 (d, J = 6.3 Hz, 1H), 6.95 (s, 1H), 7.65 (s, 1H), 7.96 (s, 1H), 8.15 (s, 1H), 8.46 (t, J = 6.3 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 468 (M⁺+1)

50 Example 334: 1-Propylbutyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0437] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-heptanol (27 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/

methanol to give the title compound (44 mg, yield 58%).

$^1\text{H-NMR}$ ($\text{CDCl}_3\text{-d}_1$, 400 MHz) : δ 0.96 (t, $J = 7.1$ Hz, 6H), 1.37 - 1.45 (m, 4H), 1.57 - 1.64 (m, 4H), 2.10 (s, 3H), 2.27 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 4.90 - 4.93 (m, 1H), 6.42 (s, 1H), 6.55 (d, $J = 6.3$ Hz, 1H), 7.02 (d, $J = 8.8$ Hz, 1H), 7.67 (s, 1H), 7.78 (brs, 1H), 8.15 (s, 1H), 8.45 (t, $J = 6.3$ Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 468 ($\text{M}^+ + 1$)

Example 335: Hexyl N-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0438] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-hexanol (27 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (69 mg, yield 82%).

$^1\text{H-NMR}$ ($\text{CDCl}_3\text{-d}_1$, 400 MHz): δ 0.91 (t, $J = 7.1$ Hz, 3H), 1.31 - 1.49 (m, 6H), 1.66 - 1.73 (m, 2H), 4.12 (s, 3H), 4.19 (s, 3H), 4.19 (t, $J = 7.1$ Hz, 2H), 6.79 (s, 1H), 7.20 (d, $J = 8.8$ Hz, 2H), 7.58 (d, $J = 8.8$ Hz, 2H), 7.62 (s, 1H), 8.15 (s, 1H), 8.79 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 427 ($\text{M}^+ + 1$)

Example 336: Hexyl N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0439] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-hexanol (24 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (54 mg, yield 68%).

$^1\text{H-NMR}$ ($\text{CDCl}_3\text{-d}_1$, 400 MHz): δ 0.92 (t, $J = 7.1$ Hz, 3H), 1.32 - 1.49 (m, 6H), 1.68 - 1.75 (m, 2H), 4.12 (s, 3H), 4.20 (s, 3H), 4.22 (t, $J = 6.8$ Hz, 2H), 7.18 (d, $J = 2.4$ Hz, 1H), 7.21 (d, $J = 2.7$ Hz, 1H), 7.33 (d, $J = 2.7$ Hz, 1H), 7.59 (s, 1H), 8.16 (s, 1H), 8.39 (d, $J = 9.0$ Hz, 1H), 8.82 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 461 ($\text{M}^+ + 1$)

Example 337: 1-Ethylbutyl N-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0440] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-hexanol (27 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (62 mg, yield 73%).

$^1\text{H-NMR}$ ($\text{CDCl}_3\text{-d}_1$, 400 MHz): δ 0.93 - 0.97 (m, 6H), 1.36 - 1.68 (m, 6H), 4.13 (s, 3H), 4.19 (s, 3H), 4.82 - 4.87 (m, 1H), 6.75 (s, 1H), 7.20 (d, $J = 9.0$ Hz, 2H), 7.59 (d, $J = 8.8$ Hz, 2H), 7.62 (s, 1H), 8.15 (s, 1H), 8.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 427 ($\text{M}^+ + 1$)

Example 338: 1-Ethylbutyl N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0441] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-hexanol (24 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract

was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (55 mg, yield 69%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.94 - 0.99 (m, 6H), 1.37 - 1.70 (m, 6H), 4.12 (s, 3H), 4.20 (s, 3H), 4.83 - 4.87 (m, 1H), 7.18 (d, J = 2.7 Hz, 1H), 7.20 (d, J = 2.7 Hz, 1H), 7.33 (d, J = 2.7 Hz, 1H), 7.59 (s, 1H), 8.16 (s, 1H), 8.42 (d, J = 9.3 Hz, 1H), 8.82 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 461 (M⁺+1)

Example 339: Phenethyl N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0442] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-phenyl-1-ethanol (28 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (18 mg, yield 22%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.03 (t, J = 7.1 Hz, 2H), 4.12 (s, 3H), 4.20 (s, 3H), 4.45 (t, J = 7.1 Hz, 2H), 7.17 (d, J = 2.4 Hz, 1H), 7.20 (d, J = 2.7 Hz, 1H), 7.29 - 7.34 (m, 6H), 7.58 (s, 1H), 8.16 (s, 1H), 8.33 (brs, 1H), 8.82 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 481 (M⁺+1)

Example 340: Cyclohexylmethyl N-[4-[(6,7-dimethoxy-4-quinazolinyl)oxylphenyl]carbamate

[0443] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclohexylmethanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (61 mg, yield 70%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.00 - 1.06, (m, 2H), 1.17 - 1.29 (m, 3H), 1.69 - 1.79 (m, 6H), 4.01 (d, J = 6.3 Hz, 2H), 4.12 (s, 3H), 4.19 (s, 3H), 6.80 (s, 1H), 7.19 (d, J = 9.0 Hz, 2H), 7.58 (d, J = 8.8 Hz, 2H), 7.62 (s, 1H), 8.15 (s, 1H), 8.79 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 439 (M⁺+1)

Example 341: Cyclohexylmethyl N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0444] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclohexylmethanol (26 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (54 mg, yield 66%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.01 - 1.07 (m, 2H), 1.18 - 1.31 (m, 3H), 1.70 - 1.82 (m, 6H), 4.04 (d, J = 6.3 Hz, 2H), 4.12 (s, 3H), 4.20 (s, 3H), 7.18 (d, J = 2.7 Hz, 1H), 7.21 (d, J = 2.7 Hz, 1H), 7.33 (d, J = 2.7 Hz, 1H), 7.59 (s, 1H), 8.16 (s, 1H), 8.39 (d, J = 9.0 Hz, 1H), 8.82 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 473 (M⁺+1)

Example 342: Cycloheptyl N-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0445] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cycloheptanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by

washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (62 mg, yield 72%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.49 - 1.77 (m, 10H), 1.97 - 2.04 (m, 2H), 4.12 (s, 3H), 4.19 (s, 3H), 4.92 - 4.99 (m, 1H), 6.74 (s, 1H), 7.19 (d, J = 9.0 Hz, 2H), 7.57 (d, J = 9.0 Hz, 2H), 7.62 (s, 1H), 8.15 (s, 1H), 8.79 (s, 1H)
Mass spectrometry value (ESI-MS, m/z) : 439 (M⁺+1)

Example 343: Cycloheptyl N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0446] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cycloheptanol (26 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (60 mg, yield 73%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.42 - 1.79 (m, 10H), 1.80 - 2.04 (m, 2H), 4.12 (s, 3H), 4.20 (s, 3H), 4.95 - 4.99 (m, 1H), 7.14 - 7.20 (m, 2H), 7.32 (d, J = 2.7 Hz, 1H), 7.59 (s, 1H), 8.16 (s, 1H), 8.40 (d, J = 8.8 Hz, 1H), 8.82 (s, 1H)
Mass spectrometry value (ESI-MS, m/z) : 473 (M⁺+1)

Example 344: Butyl N-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0447] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-butanol (19 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (46 mg, yield 58%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.97 (t, J = 7.3 Hz, 3H), 1.40 - 1.51 (m, 2H), 1.60 - 1.72 (m, 2H), 4.12 (s, 3H), 4.19 (s, 3H), 4.19 (t, J = 6.6 Hz, 2H), 6.77 (s, 1H), 7.20 (d, J = 9.0 Hz, 2H), 7.58 (d, J = 8.8 Hz, 2H), 7.62 (s, 1H), 8.14 (s, 1H), 8.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 398 (M⁺+1)

Example 345: Butyl N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0448] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-butanol (17 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (50 mg, yield 66%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.98 (t, J = 7.3 Hz, 3H), 1.40 - 1.51 (m, 2H), 1.58 - 1.74 (m, 2H), 4.12 (s, 3H), 4.20 (s, 3H), 4.23 (t, J = 6.6 Hz, 2H), 7.19 - 7.25 (m, 2H), 7.33 (d, J = 2.7 Hz, 1H), 7.59 (s, 1H), 8.15 (s, 1H), 8.39 (d, J = 8.8 Hz, 1H), 8.82 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 433 (M⁺+1)

Example 346: 1-Phenylpropyl N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0449] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-phenyl-1-propanol (31 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (46 mg, yield 58%).

roform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (43 mg, yield 51%).

¹H-NMR (CDCl₃-d₁, 400 MHz) : δ 0.96 (t, J = 7.3 Hz, 3H), 1.86 - 1.95 (m, 1H), 2.00 - 2.08 (m, 1H), 4.11 (s, 3H), 4.19 (s, 3H), 5.68 (t, J = 7.3 Hz, 1H), 7.15 - 7.17 (m, 1H), 7.25 - 7.38 (m, 5H), 7.39 (d, J = 4.6 Hz, 2H), 7.57 (s, 1H), 8.15 (s, 1H), 8.37 (d, J = 9.3 Hz, 1H), 8.81 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 495 (M⁺+1)

Example 347: Isopropyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0450] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-propanol (14 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (50 mg, yield 75%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.34 (d, J = 6.3 Hz, 6H), 2.13 (s, 3H), 2.29 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.04 - 5.07 (m, 1H), 6.38 (s, 1H), 6.58 (brs, 1H), 6.95 (s, 1H), 7.65 (s, 1H), 7.95 (s, 1H), 8.15 (s, 1H), 8.46 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 412 (M⁺+1)

Example 348: Cycloheptylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0451] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cycloheptylmethanol (33 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (64 mg, yield 77%).

¹H-NMR (CDCl₃-d₁, 400 MHz) : δ 1.23 - 1.31 (m, 2H), 1.45 - 1.60 (m, 6H), 1.70 - 1.89 (m, 5H), 4.01 (d, J = 6.8 Hz, 2H), 4.10 (s, 3H), 4.17 (s, 3H), 6.70 (d, J = 6.3 Hz, 1H), 6.80 (s, 1H), 7.18 (d, J = 9.0 Hz, 2H), 7.61 (d, J = 8.8 Hz, 2H), 7.64 (s, 1H), 8.15 (s, 1H), 8.48 (t, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 452 (M⁺+1)

Example 349: Cycloheptylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0452] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cycloheptylmethanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (64 mg, yield 83%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.23 - 1.31 (m, 2H), 1.47 - 1.59 (m, 6H), 1.70 - 1.90 (m, 5H), 2.13 (s, 3H), 2.29 (s, 3H), 4.01 (d, J = 6.8 Hz, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 6.43 (s, 1H), 6.58 (d, J = 6.3 Hz, 1H), 6.95 (s, 1H), 7.65 (s, 1H), 7.92 (brs, 1H), 8.15 (s, 1H), 8.48 (t, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 480 (M⁺+1)

Example 350: Cycloheptylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0453] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cycloheptylmethanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous

sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (77 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.19 - 1.31 (m, 2H), 1.40 - 1.90 (m, 11H), 2.10 (s, 3H), 2.28 (s, 3H), 4.01 (d, J = 6.8 Hz, 2H), 4.12 (s, 3H), 4.17 (s, 3H), 6.47 (s, 1H), 6.57 (d, J = 6.1 Hz, 1H), 7.02 (d, J = 9.0 Hz, 1H), 7.67 (s, 1H), 7.74 (brs, 1H), 8.14 (s, 1H), 8.50 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 480 (M⁺+1)

Example 351: Cycloheptylmethyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0454] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cycloheptylmethanol (33 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (41 mg, yield 46%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.22 - 1.30 (m, 2H), 1.46 - 1.88 (m, 11H), 4.00 (d, J = 6.8 Hz, 2H), 4.12 (s, 3H), 4.19 (s, 3H), 6.78 (s, 1H), 7.20 (d, J = 8.8 Hz, 2H), 7.58 (d, J = 9.0 Hz, 2H), 7.62 (s, 1H), 8.15 (s, 1H), 8.79 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 453 (M⁺+1)

Example 352: Cycloheptylmethyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0455] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cycloheptylmethanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (53 mg, yield 63%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.23 - 1.31 (m, 2H), 1.47 - 1.91 (m, 11H), 4.02 (d, J = 6.8 Hz, 2H), 4.12 (s, 3H), 4.20 (s, 3H), 7.19 (s, 1H), 7.21 (d, J = 2.7 Hz, 1H), 7.33 (d, J = 2.7 Hz, 1H), 7.59 (s, 1H), 8.15 (s, 1H), 8.39 (d, J = 9.0 Hz, 1H), 8.82 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 487 (M⁺+1)

Example 353: 2-Cyclohexylethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0456] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-cyclohexyl-1-ethanol (33 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (63 mg, yield 76%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.95 - 1.01 (m, 2H), 1.15 - 1.27 (m, 3H), 1.40 - 1.43 (m, 1H), 1.57 - 1.77 (m, 7H), 4.10 (s, 3H), 4.17 (s, 3H), 4.24 (t, J = 6.8 Hz, 2H), 6.70 (d, J = 6.3 Hz, 1H), 6.82 (s, 1H), 7.18 (d, J = 8.8 Hz, 2H), 7.61 (d, J = 8.8 Hz, 2H), 7.64 (s, 1H), 8.15 (s, 1H), 8.48 (t, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 452 (M⁺+1)

Example 354: 2-Cyclohexylethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0457] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-cyclohexyl-1-ethanol (30

mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (68 mg, yield 88%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.94 - 1.02 (m, 2H), 1.16 - 1.28 (m, 3H), 1.40 - 1.44 (m, 1H), 1.58 - 1.78 (m, 7H), 2.13 (s, 3H), 2.29 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.25 (t, J = 6.8 Hz, 2H), 6.42 (s, 1H), 6.59 (d, J = 6.6 Hz, 1H), 6.95 (s, 1H), 7.65 (s, 1H), 7.91 (s, 1H), 8.15 (s, 1H), 8.49 (t, J = 6.3 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 480 (M⁺+1)

Example 355: 2-Cyclohexylethyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0458] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-cyclohexyl-1-ethanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (65 mg, yield 84%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.93 - 1.01 (m, 2H), 1.16 - 1.24 (m, 3H), 1.27 - 1.42 (m, 1H), 1.51 - 1.77 (m, 7H), 2.10 (s, 3H), 2.28 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.24 (t, J = 6.8 Hz, 2H), 6.45 (s, 1H), 6.56 (d, J = 6.6 Hz, 1H), 7.02 (d, J = 8.8 Hz, 1H), 7.67 (s, 1H), 7.74 (brs, 1H), 8.15 (s, 1H), 8.49 (t, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 480 (M⁺+1)

Example 356: 2-Cyclohexylethyl N-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0459] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-cyclohexyl-1-ethanol (33 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (48 mg, yield 54%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.95 - 1.01 (m, 2H), 1.15 - 1.27 (m, 3H), 1.41 - 1.77 (m, 8H), 4.12 (s, 3H), 4.19 (s, 3H), 4.23 (t, J = 6.8 Hz, 2H), 6.76 (s, 1H), 7.20 (d, J = 9.0 Hz, 1H), 7.58 (d, J = 8.5 Hz, 1H), 7.62 (s, 1H), 8.15 (s, 1H), 8.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 453 (M⁺+1)

Example 357: 2-Cyclohexylethyl N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0460] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-cyclohexyl-1-ethanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (56 mg, yield 67%).

¹H-NMR (CDCl₃-d₁, 400 MHz) : δ 0.96 - 1.02 (m, 2H), 1.16 - 1.28 (m, 3H), 1.42 - 1.78 (m, 8H), 4.12 (s, 3H), 4.20 (s, 3H), 4.26 (t, J = 6.8 Hz, 2H), 7.18 (s, 1H), 7.20 (d, J = 2.7 Hz, 1H), 7.33 (d, J = 2.7 Hz, 1H), 7.59 (s, 1H), 8.16 (s, 1H), 8.39 (d, J = 9.0 Hz, 1H), 8.83 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 487 (M⁺+1)

Example 358: 1-Ethylpropyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]carbamate

[0461] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and

the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-pentanol (23 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (40 mg, yield 53%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.96 (t, J = 7.6 Hz, 6H), 1.62 - 1.71 (m, 4H), 4.10 (s, 3H), 4.17 (s, 3H), 4.75 - 4.79 (m, 1H), 6.70 (d, J = 6.6 Hz, 1H), 6.80 (s, 1H), 7.18 (d, J = 8.8 Hz, 2H), 7.62 (d, J = 9.0 Hz, 2H), 7.64 (s, 1H), 8.14 (s, 1H), 8.49 (t, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 412 (M⁺+1)

Example 359: 1-Ethylpropyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0462] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-pentanol (20 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (53 mg, yield 74%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.97 (t, J = 7.6 Hz, 6H), 1.59 - 1.70 (m, 4H), 2.13 (s, 3H), 2.30 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.76 - 4.79 (m, 1H), 6.43 (s, 1H), 6.58 (d, J = 6.3 Hz, 1H), 6.95 (s, 1H), 7.65 (s, 1H), 7.96 (s, 1H), 8.14 (s, 1H), 8.46 (t, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 440 (M⁺+1)

Example 360: 1-Ethylpropyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0463] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-pentanol (20 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (62 mg, yield 87%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.97 (t, J = 7.6 Hz, 6H), 1.59 - 1.70 (m, 4H), 2.10 (s, 3H), 2.28 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 4.76 - 4.79 (m, 1H), 6.44 (s, 1H), 6.56 (d, J = 6.3 Hz, 1H), 7.02 (d, J = 8.8 Hz, 1H), 7.67 (s, 1H), 7.78 (brs, 1H), 8.15 (s, 1H), 8.46 (t, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 440 (M⁺+1)

Example 361: 1-Ethylpropyl N-[4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0464] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-pentanol (23 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (55 mg, yield 67%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.95 (t, J = 7.6 Hz, 6H), 1.59 - 1.69 (m, 4H), 4.13 (s, 3H), 4.19 (s, 3H), 4.75 - 4.78 (m, 1H), 6.75 (s, 1H), 7.19 (d, J = 9.0 Hz, 2H), 7.59 (d, J = 9.0 Hz, 2H), 7.62 (s, 1H), 8.15 (s, 1H), 8.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 413 (M⁺+1)

Example 362: 1-Ethylpropyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0465] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-pentanol (20 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (49 mg, yield 63%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.97 (t, J = 7.6 Hz, 6H), 1.58 - 1.69 (m, 4H), 4.12 (s, 3H), 4.20 (s, 3H), 4.77 - 4.80 (m, 1H), 7.18 (s, 1H), 7.33 (d, J = 2.4 Hz, 1H), 7.59 (s, 1H), 8.16 (s, 1H), 8.42 (d, J = 9.0 Hz, 1H), 8.82 (s, 1H)
Mass spectrometry value (ESI-MS, m/z): 447 (M⁺+1)

Example 363: Cyclopentyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0466] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cyclopentanol (22 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (40 mg, yield 53%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.60 - 1.94 (m, 8H), 4.10 (s, 3H), 4.17 (s, 3H), 5.23 - 5.24 (m, 1H), 6.69 (d, J = 6.3 Hz, 1H), 6.74 (s, 1H), 7.17 (d, J = 9.0 Hz, 2H), 7.60 (d, J = 9.0 Hz, 2H), 7.64 (s, 1H), 8.15 (s, 1H), 8.48 (t, J = 6.3 Hz, 1H)
Mass spectrometry value (ESI-MS, m/z): 410 (M⁺+1)

Example 364: Cyclopentyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0467] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cyclopentanol (20 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (70 mg, yield 99%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.58 - 1.96 (m, 8H), 2.13 (s, 3H), 2.29 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.22 - 5.23 (m, 1H), 6.38 (s, 1H), 6.58 (d, J = 6.6 Hz, 1H), 6.94 (s, 1H), 7.65 (s, 1H), 7.95 (s, 1H), 8.15 (s, 1H), 8.47 (brs, 1H)
Mass spectrometry value (ESI-MS, m/z): 438 (M⁺+1)

Example 365: Cyclopentyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0468] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cyclopentanol (20 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (62 mg, yield 84%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.66 - 1.95 (m, 8H), 2.10 (s, 3H), 2.27 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.21 - 5.25 (m, 1H), 6.41 (s, 1H), 6.56 (d, J = 6.3 Hz, 1H), 7.01 (d, J = 8.8 Hz, 1H), 7.67 (s, 1H), 7.78 (d, J = 8.8 Hz, 1H), 8.15 (s, 1H), 8.47 (t, J = 6.6 Hz, 1H)
Mass spectrometry value (ESI-MS, m/z): 438 (M⁺+1)

Example 366: Cyclopentyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0469] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cyclopentanol (22 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (62 mg, yield 76%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.49 - 1.93 (m, 8H), 4.12 (s, 3H), 4.19 (s, 3H), 5.22 - 5.23 (m, 1H), 6.71 (s, 1H), 7.19 (d, J = 9.0 Hz, 2H), 7.57 (d, J = 8.8 Hz, 2H), 7.62 (s, 1H), 8.15 (s, 1H), 8.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 410 (M⁺+1)

Example 367: Cyclopentyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0470] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cyclopentanol (20 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (62 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.49 - 1.99 (m, 8H), 4.12 (s, 3H), 4.20 (s, 3H), 5.23 - 5.27 (m, 1H), 7.13 (s, 1H), 7.19 (dd, J = 2.9, 9.0 Hz, 1H), 7.32 (d, J = 2.7 Hz, 1H), 7.59 (s, 1H), 8.16 (s, 1H), 8.40 (d, J = 9.0 Hz, 1H), 8.82 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 445 (M⁺+1)

Example 368: 1-Butylpentyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0471] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 5-nonanol (38 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (2 mg, yield 2%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.92 (t, J = 7.1 Hz, 6H), 1.31 - 1.39 (m, 8H), 1.57 - 1.64 (m, 4H), 4.11 (s, 3H), 4.17 (s, 3H), 4.85 - 4.91 (m, 1H), 6.69 (d, J = 6.8 Hz, 1H), 7.18 (d, J = 9.0 Hz, 2H), 7.61 (d, J = 8.8 Hz, 2H), 7.64 (s, 1H), 8.15 (d, J = 3.9 Hz, 1H), 8.46 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 468 (M⁺+1)

Example 369: 1-Butylpentyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0472] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 5-nonanol (33 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (56 mg, yield 70%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.93 (t, J = 7.1 Hz, 6H), 1.37 - 1.39 (m, 8H), 1.61 (brs, 1H), 2.13 (s, 3H), 2.29 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.87 - 4.90 (m, 1H), 6.41 (s, 1H), 6.58 (d, J = 6.6 Hz, 1H), 6.95 (s, 1H), 7.65 (s, 1H), 7.97 (s, 1H), 8.15 (d, J = 3.9 Hz, 1H), 8.46 (t, J = 6.3 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 496 (M⁺+1)

Example 370: 1-Butylpentyll N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0473] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 5-nonanol (33 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (57 mg, yield 72%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.92 (t, J = 7.1 Hz, 6H), 1.36 (brs, 8H), 1.56 - 1.60 (m, 4H), 2.10 (s, 3H), 2.28 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 4.87 - 4.90 (m, 1H), 6.42 (s, 1H), 6.55 (d, J = 6.1 Hz, 1H), 7.02 (d, J = 8.8 Hz, 1H), 7.67 (s, 1H), 7.80 (brs, 1H), 8.16 (d, J = 3.9 Hz, 1H), 8.45 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 496 (M⁺+1)

Example 371: 1-Butylpentyll N-{4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}carbamate

[0474] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 5-nonanol (38 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (40 mg, yield 44%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.90 - 0.93 (m, 6H), 1.34 - 1.35 (m, 8H), 1.59 (brs, 4H), 4.13 (s, 3H), 4.19 (s, 3H), 4.86 - 4.89 (m, 1H), 6.71 (s, 1H), 7.19 (d, J = 9.0 Hz, 2H), 7.59 (d, J = 8.8 Hz, 2H), 7.62 (s, 1H), 8.15 (s, 1H), 8.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 469 (M⁺+1)

Example 372: 1-Butylpentyll N-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}carbamate

[0475] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 5-nonanol (33 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (42 mg, yield 49%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.92 (t, J = 7.1 Hz, 6H), 1.36 (brs, 8H), 1.61 (brs, 4H), 4.13 (s, 3H), 4.20 (s, 3H), 4.88 - 4.91 (m, 1H), 7.17 (s, 1H), 7.20 (s, 1H), 7.33 (s, 1H), 7.59 (s, 1H), 8.17 (s, 1H), 8.43 (d, J = 9.0 Hz, 1H), 8.82 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 503 (M⁺+1)

Example 373: Allyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0476] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-propen-1-ol (13 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (56 mg, yield 84%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.13 (s, 3H), 2.29 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.71 (d, J = 5.9 Hz, 2H), 5.32 (dd, J = 1.2, 10.5 Hz, 1H), 5.40 (dd, J = 1.5, 17.3 Hz, 1H), 5.96 - 6.06 (m, 1H), 6.49 (s, 1H), 6.59 (d, J = 6.6 Hz, 1H), 6.96 (s, 1H), 7.65 (s, 1H), 7.91 (s, 1H), 8.16 (d, J = 3.9 Hz, 1H), 8.49 (t, J = 7.3 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 410 (M⁺+1)

Example 374: Allyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0477] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-propen-1-ol (13 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (50 mg, yield 75%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.10 (s, 3H), 2.28 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 4.71 (d, J = 5.9 Hz, 2H), 5.31 (d, J = 10.2 Hz, 1H), 5.40 (d, J = 17.3 Hz, 1H), 5.96 - 6.04 (m, 1H), 6.50 (s, 1H), 6.56 (d, J = 6.1 Hz, 1H), 7.03 (d, J = 8.8 Hz, 1H), 7.67 (s, 1H), 7.76 (s, 1H), 8.16 (d, J = 3.9 Hz, 1H), 8.48 (t, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 410 (M⁺+1)

Example 375: Allyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0478] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-propen-1-ol (15 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (42 mg, yield 54%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 4.13 (s, 3H), 4.19 (s, 3H), 4.70 (d, J = 5.9 Hz, 2H), 5.29 (dd, J = 1.2, 10.5 Hz, 1H), 5.39 (dd, J = 1.5, 17.3 Hz, 1H), 5.93 - 6.03 (m, 1H), 6.81 - 6.87 (m, 1H), 7.20 (d, J = 9.0 Hz, 2H), 7.59 (d, J = 8.8 Hz, 2H), 7.62 (s, 1H), 8.15 (s, 1H), 8.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 382 (M⁺+1)

Example 376: 3-Phenylpropyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0479] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-phenyl-1-propanol (35 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (54 mg, yield 64%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.01 - 2.08 (m, 2H), 2.75 (t, J = 8.1 Hz, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 4.24 (t, J = 6.6 Hz, 2H), 6.70 (d, J = 6.3 Hz, 1H), 6.80 (s, 1H), 7.17 - 7.33 (m, 7H), 7.61 (d, J = 8.8 Hz, 2H), 7.64 (s, 1H), 8.15 (d, J = 3.7 Hz, 1H), 8.50 (t, J = 6.8 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 460 (M⁺+1)

Example 377: 3-Phenylpropyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0480] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-phenyl-1-propanol (31 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (77 mg, yield 98%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.02 - 2.09 (m, 2H), 2.13 (s, 3H), 2.29 (s, 3H), 2.76 (t, J = 7.8 Hz, 2H), 4.11 (s,

3H), 4.17 (s, 3H), 4.25 (t, J = 6.6 Hz, 2H), 6.41 (s, 1H), 6.59 (d, J = 6.3 Hz, 1H), 6.95 (s, 1H), 7.22 - 7.33 (m, 5H), 7.65 (s, 1H), 7.91 (s, 1H), 8.15 (d, J = 3.7 Hz, 1H), 8.49 (t, J = 6.8 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 488 (M⁺+1)

5 Example 378: 3-Phenylpropyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0481] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-phenyl-1-propanol (31 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (56 mg, yield 71%).

15 ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.01 - 2.09 (m, 2H), 2.11 (s, 3H), 2.28 (s, 3H), 2.75 (t, J = 8.1 Hz, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 4.24 (t, J = 6.6 Hz, 2H), 6.43 (s, 1H), 6.56 (d, J = 6.6 Hz, 1H), 7.03 (d, J = 8.8 Hz, 1H), 7.21 - 7.33 (m, 5H), 7.67 (s, 1H), 7.75 (brs, 1H), 8.16 (d, J = 3.9 Hz, 1H), 8.49 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 488 (M⁺+1)

20 Example 379: 3-Phenylpropyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0482] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-phenyl-1-propanol (31 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (42 mg, yield 49%).

30 ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.04 - 2.08 (m, 2H), 2.76 (t, J = 8.3 Hz, 2H), 4.12 (s, 3H), 4.20 (s, 3H), 4.26 (t, J = 6.6 Hz, 2H), 7.18 - 7.34 (m, 8H), 7.59 (s, 1H), 8.17 (s, 1H), 8.38 (d, J = 8.8 Hz, 1H), 8.83 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 495 (M⁺+1)

Example 380: Cyclopropylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

35 [0483] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclopropylmethanol (19 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (25 mg, yield 34%).

40 ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.33 - 0.37 (m, 2H), 0.60 - 0.65 (m, 2H), 1.18 - 1.22 (m, 1H), 4.04 (d, J = 7.3 Hz, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 6.71 (s, 1H), 6.85 (s, 1H), 7.18 (d, J = 8.5 Hz, 2H), 7.61 (d, J = 8.3 Hz, 2H), 7.65 (s, 1H), 8.14 (s, 3H), 8.51 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 395 (M⁺+1)

Example 381: Cyclopropylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

50 [0484] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclopropylmethanol (17 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (51 mg, yield 74%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.34 - 0.38 (m, 2H), 0.61 - 0.66 (m, 2H), 1.18 - 1.24 (m, 1H), 2.13 (s, 3H), 2.30 (s, 3H), 4.04 (d, J = 7.3 Hz, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 6.47 (s, 1H), 6.59 (s, 1H), 6.95 (s, 1H), 7.65 (s, 1H), 7.92 (s, 1H), 8.15 (s, 1H), 8.48 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 424 (M⁺+1)

Example 382: Cyclopropylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0485] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclopropylmethanol (17 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (55 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.34 - 0.38 (m, 2H), 0.61 - 0.66 (m, 2H), 1.19 - 1.23 (m, 1H), 2.11 (s, 3H), 2.28 (s, 3H), 4.04 (d, J = 7.3 Hz, 2H), 4.12 (s, 3H), 4.17 (s, 3H), 6.50 (s, 1H), 6.56 (s, 1H), 7.03 (d, J = 8.8 Hz, 1H), 7.67 (s, 1H), 7.78 (s, 1H), 8.15 (s, 1H), 8.48 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 424 (M⁺+1)

Example 383: Cyclopropylmethyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0486] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclopropylmethanol (19 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (60 mg, yield 75%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.33 - 0.36 (m, 2H), 0.59 - 0.64 (m, 2H), 1.16 - 1.23 (m, 1H), 4.03 (d, J = 7.6 Hz, 2H), 4.12 (s, 3H), 4.17 (s, 3H), 6.81 (s, 1H), 7.20 (d, J = 9.0 Hz, 2H), 7.57 (d, J = 8.5 Hz, 2H), 7.61 (s, 1H), 7.99 (s, 1H), 8.77 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 396 (M⁺+1)

Example 384: Cyclopropylmethyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0487] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclopropylmethanol (17 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (49 mg, yield 65%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.34 - 0.38 (m, 2H), 0.62 - 0.66 (m, 2H), 1.20 - 1.24 (m, 1H), 4.06 (d, J = 7.3 Hz, 2H), 4.12 (s, 3H), 4.20 (s, 3H), 7.19 - 7.21 (m, 2H), 7.33 (s, 1H), 7.59 (s, 1H), 8.17 (s, 1H), 8.40 (d, J = 8.8 Hz, 1H), 8.83 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 431 (M⁺+1)

Example 385: Cyclobutylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0488] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclobutylmethanol (22 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried

over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (48 mg, yield 64%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.80 - 2.13 (m, 6H), 2.65 - 2.71 (m, 1H), 4.10 (s, 3H), 4.17 (s, 3H), 4.18 (d, J = 6.8 Hz, 2H), 6.70 (s, 1H), 6.80 (s, 1H), 7.18 (d, J = 8.8 Hz, 2H), 7.60 (d, J = 8.5 Hz, 2H), 7.64 (s, 1H), 8.14 (s, 1H), 8.50 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 410 (M⁺+1)

Example 386: Cyclobutylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0489] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclobutylmethanol (20 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (61 mg, yield 86%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.81 - 1.99 (m, 4H), 2.05 - 2.20 (m, 2H), 2.13 (s, 3H), 2.29 (s, 3H), 2.66 - 2.73 (m, 1H), 4.11 (s, 3H), 4.17 (s, 3H), 4.19 (d, J = 7.1 Hz, 2H), 6.43 (s, 1H), 6.60 (s, 1H), 7.95 (s, 1H), 7.65 (s, 1H), 7.91 (s, 1H), 8.15 (s, 1H), 8.49 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 438 (M⁺+1)

Example 387: Cyclobutylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0490] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclobutylmethanol (20 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (59 mg, yield 83%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.78 - 2.08 (m, 6H), 2.08 (s, 3H), 2.26 (s, 3H), 2.60 - 2.70 (m, 1H), 4.09 (s, 3H), 4.15 (s, 3H), 4.16 (d, J = 6.8 Hz, 2H), 6.43 (s, 1H), 6.55 (s, 1H), 7.00 (d, J = 8.5 Hz, 1H), 7.65 (s, 1H), 7.74 (brs, 1H), 8.13 (s, 1H), 8.47 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 438 (M⁺+1)

Example 388: Cyclobutylmethyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0491] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclobutylmethanol (22 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (55 mg, yield 67%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.80 - 1.99 (m, 4H), 2.07 - 2.14 (m, 2H), 2.64 - 2.71 (m, 1H), 4.12 (s, 3H), 4.17 (d, J = 6.8 Hz, 2H), 4.19 (s, 3H), 6.79 (s, 1H), 7.20 (d, J = 8.8 Hz, 2H), 7.58 (d, J = 8.3 Hz, 2H), 7.62 (s, 1H), 8.11 (s, 1H), 8.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 410 (M⁺+1)

Example 389: Cyclobutylmethyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0492] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclobutylmethanol (20 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous

sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (46 mg, yield 59%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.81 - 2.01 (m, 4H), 2.09 - 2.17 (m, 2H), 2.66 - 2.74 (m, 1H), 4.12 (s, 3H), 4.20 (d, J = 6.8 Hz, 2H), 4.20 (s, 3H), 7.19 (s, 1H), 7.21 (d, J = 2.7 Hz, 1H), 7.33 (d, J = 2.4 Hz, 1H), 7.59 (s, 1H), 8.17 (s, 1H), 8.39 (d, J = 9.3 Hz, 1H), 8.83 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 445 (M⁺+1)

Example 390: Cyclohexyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2,5-dimethylphenyl}carbamate

[0493] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cyclohexanol (23 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (58 mg, yield 74%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.29 - 1.58 (m, 6H), 1.74 - 1.81 (m, 2H), 1.95 - 2.00 (m, 2H), 2.12 (s, 3H), 2.29 (s, 3H), 4.13 (s, 3H), 4.20 (s, 3H), 4.76 - 4.77 (m, 1H), 6.38 (s, 1H), 6.95 (s, 1H), 7.62 (s, 1H), 7.93 (s, 1H), 8.16 (s, 1H), 8.79 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 453 (M⁺+1)

Example 391: Cyclohexyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2,3-dimethylphenyl}carbamate

[0494] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cyclohexanol (23 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (50 mg, yield 64%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.21 - 1.57 (m, 6H), 1.73 - 1.79 (m, 2H), 1.94 - 2.00 (m, 2H), 2.08 (s, 3H), 2.27 (s, 3H), 4.14 (s, 3H), 4.20 (s, 3H), 4.70 - 4.80 (m, 1H), 6.40 (s, 1H), 7.01 (d, J = 8.8 Hz, 1H), 7.65 (s, 1H), 7.78 (brs, 1H), 8.16 (s, 1H), 8.78 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 453 (M⁺+1)

Example 392: Cyclopentyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2,5-dimethylphenyl}carbamate

[0495] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cyclopentanol (20 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (47 mg, yield 61%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.49 - 1.84 (m, 6H), 1.89 - 1.98 (m, 2H), 2.12 (s, 3H), 2.28 (s, 3H), 4.13 (s, 3H), 4.20 (s, 3H), 5.21 - 5.22 (m, 1H), 6.36 (s, 1H), 6.95 (s, 1H), 7.62 (s, 1H), 7.93 (s, 1H), 8.16 (s, 1H), 8.79 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 439 (M⁺+1)

Example 393: Cyclopentyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2,3-dimethylphenyl}carbamate

[0496] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cyclopentanol

(20 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (43 mg, yield 56%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.49 - 1.83 (m, 6H), 1.88 - 1.97 (m, 2H), 2.08 (s, 3H), 2.26 (s, 3H), 4.14 (s, 3H), 4.20 (s, 3H), 5.20 - 5.25 (m, 1H), 6.39 (s, 1H), 7.01 (d, J = 8.8 Hz, 1H), 7.65 (s, 1H), 7.77 (brs, 1H), 8.16 (s, 1H), 8.78 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 439 (M⁺+1)

Example 394: Cyclopentylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0497] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclopentylmethanol (26 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (42 mg, yield 54%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.22 - 1.84 (m, 8H), 2.25 - 2.29 (m, 1H), 4.10 - 4.17 (m, 8H), 6.69 (d, J = 6.1 Hz, 1H), 6.80 (s, 1H), 7.18 (d, J = 9.0 Hz, 2H), 7.61 (d, J = 8.5 Hz, 2H), 7.64 (s, 1H), 8.15 (s, 1H), 8.47 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 424 (M⁺+1)

Example 395: Cyclopentylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0498] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclopentylmethanol (23 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (62 mg, yield 85%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.31 - 1.68 (m, 6H), 1.78 - 1.86 (m, 2H), 2.13 (s, 3H), 2.20 - 2.30 (m, 1H), 2.29 (s, 3H), 4.10 (d, J = 6.3 Hz, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 6.42 (s, 1H), 6.58 (d, J = 6.3 Hz, 1H), 6.95 (s, 1H), 7.65 (s, 1H), 7.91 (s, 1H), 8.16 (s, 1H), 8.46 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 452 (M⁺+1)

Example 396: Cyclopentylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0499] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclopentylmethanol (23 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (48 mg, yield 66%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.27 - 1.35 (m, 2H), 1.55 - 1.67 (m, 4H), 1.76 - 1.84 (m, 2H), 2.10 (s, 3H), 2.26 - 2.30 (m, 1H), 2.28 (s, 3H), 4.09 (d, J = 7.1 Hz, 2H), 4.12 (s, 3H), 4.18 (s, 3H), 6.44 (s, 1H), 6.56 (s, 1H), 7.03 (d, J = 8.5 Hz, 1H), 7.67 (s, 1H), 7.76 (brs, 1H), 8.16 (s, 1H), 8.45 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 452 (M⁺+1)

Example 397: Cyclopentylmethyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0500] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride

was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclopentylmethanol (26 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (64 mg, yield 75%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.30 - 1.33 (m, 2H), 1.59 - 1.65 (m, 4H), 1.76 - 1.83 (m, 2H), 4.09 (d, J = 7.3 Hz, 2H), 4.12 (s, 3H), 4.19 (s, 3H), 6.76 (s, 1H), 7.20 (d, J = 9.0 Hz, 2H), 7.58 (d, J = 8.8 Hz, 2H), 7.62 (s, 1H), 8.15 (s, 1H), 8.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 425 (M⁺+1)

Example 398: Cyclopentylmethyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0501] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cyclopentylmethanol (23 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (47 mg, yield 59%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.29 - 1.34 (m, 2H), 1.57 - 1.66 (m, 4H), 1.77 - 1.85 (m, 2H), 4.11 (d, J = 7.1 Hz, 2H), 4.12 (s, 3H), 4.20 (s, 3H), 7.19 (s, 1H), 7.33 (d, J = 2.7 Hz, 1H), 7.59 (s, 1H), 8.17 (s, 1H), 8.39 (d, J = 9.0 Hz, 1H), 8.82 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 459 (M⁺+1)

Example 399: 2-Morpholinoethyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0502] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-morpholino-1-ethanol (34 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (54 mg, yield 60%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.94 - 3.04 (m, 2H), 3.30 - 3.36 (m, 2H), 3.58 - 3.63 (m, 2H), 4.01 - 4.07 (m, 2H), 4.12 (s, 3H), 4.19 (s, 3H), 4.53 - 4.59 (m, 4H), 7.19 (d, J = 9.0 Hz, 2H), 7.62 (s, 1H), 7.67 (d, J = 9.0 Hz, 2H), 8.14 (s, 1H), 8.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 456 (M⁺+1)

Example 400: 1-Propylbutyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0503] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-heptanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (53 mg, yield 61%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.95 (t, J = 7.3 Hz, 6H), 1.19 - 1.62 (m, 8H), 4.13 (s, 3H), 4.19 (s, 3H), 4.90 - 4.93 (m, 1H), 6.72 (s, 1H), 7.19 (d, J = 9.0 Hz, 2H), 7.58 (d, J = 8.8 Hz, 2H), 7.62 (s, 1H), 8.15 (s, 1H), 8.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 441 (M⁺+1)

Example 401: 1-Ethylpentyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0504] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml),

and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-heptanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (63 mg, yield 72%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.92 - 0.97 (m, 6H), 1.34 - 1.67 (m, 8H), 4.13 (s, 3H), 4.19 (s, 3H), 4.81 - 4.84 (m, 1H), 6.72 (s, 1H), 7.19 (d, J = 9.0 Hz, 2H), 7.58 (d, J = 9.0 Hz, 2H), 7.62 (s, 1H), 8.15 (s, 1H), 8.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 441 (M⁺+1)

Example 402: 2-(Tert-butyl)phenyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0505] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-(tert-butyl)phenol (39 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (74 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.41 (s, 9H), 4.13 (s, 3H), 4.19 (s, 3H), 7.08 - 7.11 (m, 1H), 7.19 - 7.29 (m, 5H), 7.41 - 7.44 (m, 1H), 7.63 (s, 1H), 7.70 (d, J = 8.5 Hz, 2H), 8.15 (s, 1H), 8.79 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 475 (M⁺+1)

Example 403: 2-Methoxyphenyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0506] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-methoxyphenol (32 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (16 mg, yield 18%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.87 (s, 3H), 4.13 (s, 3H), 4.19 (s, 3H), 6.97 - 7.02 (m, 2H), 7.15 - 7.26 (m, 5H), 7.62 (s, 1H), 7.66 (d, J = 8.8 Hz, 2H), 8.16 (s, 1H), 8.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 448 (M⁺+1)

Example 404: 2-Methylallyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0507] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-methyl-2-propen-1-ol (19 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (38 mg, yield 52%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.82 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.63 (s, 2H), 4.99 (s, 1H), 5.06 (s, 1H), 6.70 (d, J = 6.3 Hz, 1H), 6.87 (s, 1H), 7.19 (d, J = 9.0 Hz, 2H), 7.62 (d, J = 9.0 Hz, 2H), 7.64 (s, 1H), 8.15 (s, 1H), 8.48 (t, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 395 (M⁺+1)

Example 405: 2-Methylallyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0508] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene

chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-methyl-2-propen-1-ol (17 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (31 mg, yield 45%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.83 (s, 3H), 2.13 (s, 3H), 2.30 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.64 (s, 2H), 5.00 (s, 1H), 5.06 (s, 1H), 6.59 (s, 1H), 6.96 (s, 1H), 7.65 (s, 1H), 8.16 (s, 1H), 8.46 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 424 (M⁺+1)

Example 406: 2-Methylallyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0509] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-methyl-2-propen-1-ol (17 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (40 mg, yield 58%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.83 (s, 3H), 2.11 (s, 3H), 2.29 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 4.63 (s, 2H), 5.00 (s, 1H), 5.06 (s, 1H), 6.56 (d, J = 5.9 Hz, 1H), 7.03 (d, J = 8.8 Hz, 1H), 7.67 (s, 1H), 8.16 (s, 1H), 8.46 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 424 (M⁺+1)

Example 407: 2-Methylallyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0510] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-methyl-2-propen-1-ol (19 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (37 mg, yield 47%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 4.13 (s, 3H), 4.19 (s, 3H), 4.62 (s, 2H), 4.98 (s, 1H), 5.05 (s, 1H), 6.87 (s, 1H), 7.21 (d, J = 9.0 Hz, 2H), 7.59 (d, J = 9.0 Hz, 2H), 7.62 (s, 1H), 8.15 (s, 1H), 8.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 396 (M⁺+1)

Example 408: 1-Ethyl-3-butyryl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0511] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 5-hexyn-3-ol (26 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (30 mg, yield 39%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.01 (t, J = 7.6 Hz, 3H), 1.79 - 1.83 (m, 2H), 2.04 - 2.05 (m, 1H), 2.57 - 2.61 (m, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 4.90 - 4.93 (m, 1H), 6.69 (d, J = 6.1 Hz, 1H), 6.83 (s, 1H), 7.19 (d, J = 9.0 Hz, 2H), 7.61 (d, J = 8.8 Hz, 2H), 7.64 (s, 1H), 8.15 (s, 1H), 8.47 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 422 (M⁺+1)

Example 409: 1-Ethyl-3-butyryl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0512] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 5-hexyn-3-ol (23 mg) was

added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (52 mg, yield 72%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.01 (t, J = 7.6 Hz, 3H), 1.79 - 1.83 (m, 2H), 2.05 (s, 1H), 2.13 (s, 3H), 2.30 (s, 3H), 2.55 - 2.60 (m, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 4.92 - 4.93 (m, 1H), 6.48 (s, 1H), 6.59 (s, 1H), 6.96 (s, 1H), 7.65 (s, 1H), 7.93 (s, 1H), 8.15 (s, 1H), 8.47 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 450 (M⁺+1)

Example 410: 1-Ethyl-3-butynyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0513] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 5-hexyn-3-ol (23 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (43 mg, yield 59%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.01 (t, J = 7.6 Hz, 3H), 1.79 - 1.81 (m, 2H), 2.04 - 2.05 (m, 1H), 2.11 (s, 3H), 2.29 (s, 3H), 2.57 - 2.61 (m, 2H), 4.12 (s, 3H), 4.17 (s, 3H), 4.90 - 4.93 (m, 1H), 6.50 (s, 1H), 6.56 (d, J = 6.3 Hz, 1H), 7.03 (d, J = 9.0 Hz, 1H), 7.67 (s, 1H), 7.75 (s, 1H), 8.16 (s, 1H), 8.45 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 450 (M⁺+1)

Example 411: 1-Methylhexyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0514] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-heptanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (25 mg, yield 31%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.91 (t, J = 7.1 Hz, 3H), 1.26 - 1.32 (m, 11H), 4.11 (s, 3H), 4.17 (s, 3H), 4.92 - 4.96 (m, 1H), 6.70 (s, 1H), 6.72 (s, 1H), 7.18 (d, J = 8.5 Hz, 2H), 7.61 (d, J = 8.3 Hz, 2H), 7.64 (s, 1H), 8.15 (s, 1H), 8.46 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 440 (M⁺+1)

Example 412: 1-Methylhexyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0515] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-heptanol (27 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (54 mg, yield 72%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.91 (t, J = 7.1 Hz, 3H), 1.31 - 1.32 (m, 11H), 2.13 (s, 3H), 2.29 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 4.93 - 4.95 (m, 1H), 6.39 (s, 1H), 6.58 (d, J = 5.6 Hz, 1H), 6.95 (s, 1H), 7.65 (s, 1H), 7.96 (s, 1H), 8.15 (s, 1H), 8.45 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 468 (M⁺+1)

Example 413: 1-Methylhexyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0516] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine

(0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-heptanol (27 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (49 mg, yield 65%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.91 (t, J = 6.6 Hz, 3H), 1.30 - 1.32 (m, 11H), 2.12 (s, 3H), 2.29 (s, 3H), 4.12 (s, 3H), 4.18 (s, 3H), 4.93 - 4.94 (m, 1H), 6.41 (s, 1H), 7.03 (s, 1H), 7.67 (s, 1H), 7.79 (s, 1H), 8.15 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 468 (M⁺+1)

Example 414: 3-Piperidinopropyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0517] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-piperidino-1-propanol (33 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (90 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.26 (s, 4H), 1.87 - 1.96 (m, 2H), 2.13 (s, 3H), 2.29 - 2.42 (m, 2H), 2.33 (s, 3H), 2.64 - 2.73 (m, 2H), 3.11 - 3.16 (m, 2H), 3.61 - 3.63 (m, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 4.31 (t, J = 5.6 Hz, 2H), 6.59 (d, J = 6.6 Hz, 1H), 6.96 (s, 1H), 7.65 (s, 1H), 7.84 (s, 1H), 8.15 (s, 1H), 8.47 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 495 (M⁺+1)

Example 415: 3-Piperidinopropyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0518] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-piperidino-1-propanol (33 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (62 mg, yield 73%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.62 (brs, 8H), 2.01 (brs, 2H), 2.13 (s, 3H), 2.27 (s, 3H), 3.00 (brs, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 4.29 (t, J = 5.9 Hz, 2H), 6.27 (d, J = 5.1 Hz, 1H), 6.99 (d, J = 8.8 Hz, 1H), 7.44 (s, 1H), 7.57 (s, 1H), 7.61 (s, 1H), 8.44 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 495 (M⁺+1)

Example 416: 1,3-Dioxo-2,3-dihydro-1H-2-isoindolyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0519] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-hydroxy-1,3-isoindolinedione (42 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (11 mg, yield 12%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 4.12 (s, 3H), 4.18 (s, 3H), 6.83 (d, J = 6.1 Hz, 1H), 7.39 (d, J = 9.0 Hz, 2H), 7.66 (s, 1H), 7.72 (d, J = 9.0 Hz, 2H), 7.85 - 7.87 (m, 2H), 8.00 - 8.02 (m, 3H), 8.19 (s, 1H), 8.52 - 8.53 (m, 1H)

Mass spectrometry value (ESI-MS, m/z): 486 (M⁺+1)

Example 417: (1,3-Dioxo-2,3-dihydro-1H-2-isoindolyl)methyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0520] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-(hydroxymethyl)-1,3-isoindolinedione (41 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (48 mg, yield 57%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.13 (s, 3H), 2.25 (s, 3H), 3.10 - 3.11 (m, 1H), 4.10 (s, 3H), 4.17 (s, 3H), 5.87 (s, 1H), 6.50 (s, 1H), 6.55 (s, 1H), 6.94 (s, 1H), 7.64 (s, 1H), 7.81 - 7.83 (m, 2H), 7.96 - 7.98 (m, 2H), 8.15 (s, 1H), 8.46 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 529 (M⁺+1)

Example 418: (1,3-Dioxo-2,3-dihydro-1H-2-isoindolyl)methyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0521] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-(hydroxymethyl)-1,3-isoindolinedione (41 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (14 mg, yield 17%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.09 (s, 3H), 2.24 (s, 3H), 3.10 - 3.11 (m, 1H), 4.11 (s, 3H), 4.17 (s, 3H), 5.27 (s, 1H), 5.87 (s, 1H), 6.53 (s, 1H), 7.01 - 7.04 (m, 1H), 7.66 - 7.96 (m, 7H)

Mass spectrometry value (ESI-MS, m/z): 529 (M⁺+1)

Example 419: 2-(1,3-Dioxo-2,3-dihydro-1H-2-isoindolyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0522] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-(2-hydroxyethyl)-1,3-isoindolinedione (44 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (57 mg, yield 66%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.10 (s, 3H), 2.26 (s, 3H), 4.05 (t, J = 5.1 Hz, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 4.46 (t, J = 5.4 Hz, 2H), 6.42 (s, 1H), 6.59 (d, J = 6.3 Hz, 1H), 6.94 (s, 1H), 7.64 (s, 1H), 7.75 - 7.77 (m, 3H), 7.87 - 7.89 (m, 2H), 8.15 (s, 1H), 8.47 (t, J = 6.3 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 543 (M⁺+1)

Example 420: 2-(1,3-Dioxo-2,3-dihydro-1H-2-isoindolyl)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0523] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-(2-hydroxyethyl)-1,3-isoindolinedione (44 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (21 mg, yield 24%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.08 (s, 3H), 2.24 (s, 3H), 4.05 (t, J = 5.1 Hz, 2H), 4.11 (s, 3H), 4.17 (s, 3H), 4.46 (t, J = 5.4 Hz, 2H), 6.45 (s, 1H), 6.55 (s, 1H), 6.99 (d, J = 8.5 Hz, 1H), 7.66 (s, 2H), 7.74 - 7.76 (m, 2H), 7.86 - 7.88 (m, 2H), 8.16 (s, 1H), 8.46 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 543 (M⁺+1)

Example 421: 3-Morpholinopropyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0524] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-morpholino-1-propanol (38 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (38 mg, yield 41%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.89 - 1.96 (m, 2H), 2.51 - 2.53 (m, 6H), 3.76 (t, J = 4.9 Hz, 4H), 4.05 (s, 3H), 4.06 (s, 3H), 4.27 (t, J = 6.6 Hz, 2H), 6.45 (d, J = 5.4 Hz, 1H), 6.74 (s, 1H), 7.15 (d, J = 9.0 Hz, 2H), 7.45 (s, 1H), 7.49 (d, J = 8.8 Hz, 2H), 7.56 (s, 1H), 8.48 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 469 (M⁺+1)

Example 422: 3-Morpholinopropyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0525] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-morpholino-1-propanol (33 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (56 mg, yield 66%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.89 - 1.96 (m, 2H), 2.15 (s, 3H), 2.25 (s, 3H), 2.50 (brs, 6H), 3.75 (t, J = 4.6 Hz, 4H), 4.057 (s, 3H), 4.063 (s, 3H), 4.27 (t, J = 6.6 Hz, 2H), 6.30 (d, J = 5.1 Hz, 1H), 6.38 (s, 1H), 6.93 (s, 1H), 7.45 (s, 1H), 7.59 (s, 1H), 7.77 (s, 1H), 8.45 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 497 (M⁺+1)

Example 423: 3-Morpholinopropyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0526] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-morpholino-1-propanol (33 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (66 mg, yield 77%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.10 (s, 3H), 2.31 (s, 3H), 2.39 (brs, 2H), 2.93 (brs, 2H), 3.22 (brs, 2H), 3.53 (brs, 2H), 4.00 - 4.03 (m, 2H), 4.12 (s, 3H), 4.17 (s, 3H), 4.32 (brs, 4H), 6.57 (s, 1H), 7.01 (brs, 1H), 7.67 (s, 2H), 8.14 (s, 1H), 8.50 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 497 (M⁺+1)

Example 424: 3-(4-Methylpiperazino)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0527] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-(4-methylpiperazino)-1-propanol (41 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium

sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (9 mg, yield 9%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.89 - 1.93 (m, 2H), 2.39 (s, 3H), 2.49 - 2.62 (m, 10H), 4.05 (s, 6H), 4.25 (t, J = 6.3 Hz, 2H), 6.44 (d, J = 5.4 Hz, 1H), 6.79 (s, 1H), 7.15 (d, J = 8.8 Hz, 2H), 7.42 (s, 1H), 7.49 (d, J = 8.5 Hz, 2H), 7.56 (s, 1H), 8.48 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 482 (M⁺+1)

Example 425: 3-(4-Methylpiperazino)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0528] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-(4-methylpiperazino)-1-propanol (36 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (33 mg, yield 36%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.90 - 1.95 (m, 2H), 2.15 (s, 3H), 2.25 (s, 3H), 2.35 (s, 3H), 2.42 - 2.53 (m, 10H), 4.05 (s, 3H), 4.06 (s, 3H), 4.25 (t, J = 6.3 Hz, 2H), 6.29 (d, J = 5.4 Hz, 1H), 6.38 (s, 1H), 6.92 (s, 1H), 7.42 (s, 1H), 7.59 (s, 1H), 7.75 (s, 1H), 8.45 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 509 (M⁺+1)

Example 426: 3-(Diethylamino)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0529] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-(diethylamino)-1-propanol (34 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (32 mg, yield 36%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.39 (t, J = 7.1 Hz, 6H), 2.20 - 2.22 (m, 2H), 3.14 - 3.16 (m, 6H), 4.04 (s, 6H), 4.30 (t, J = 5.6 Hz, 2H), 6.44 (d, J = 5.1 Hz, 1H), 7.12 (d, J = 8.8 Hz, 2H), 7.42 (s, 1H), 7.56 (s, 1H), 7.64 (d, J = 8.1 Hz, 2H), 7.47 (d, J = 5.1 Hz, 1H), 8.77 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 455 (M⁺+1)

Example 427: 3-(Diethylamino)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0530] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-(diethylamino)-1-propanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (50 mg, yield 61%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.32 (t, J = 7.1 Hz, 6H), 2.14 (s, 3H), 2.17 - 2.19 (m, 2H), 2.28 (s, 3H), 2.94 - 3.01 (m, 6H), 4.05 (s, 3H), 4.06 (s, 3H), 4.30 (t, J = 5.9 Hz, 2H), 6.30 (d, J = 5.4 Hz, 1H), 6.93 (s, 1H), 7.11 (s, 1H), 7.42 (s, 1H), 7.59 (s, 1H), 7.68 (s, 1H), 8.44 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 483 (M⁺+1)

Example 428: 3-(Diethylamino)propyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0531] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-(diethylamino)-1-propanol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous

sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (65 mg, yield 78%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.47 (t, J = 7.1 Hz, 6H), 2.09 (s, 3H), 2.30 (s, 2H), 2.33 (s, 3H), 3.24 (brs, 6H), 4.12 (s, 3H), 4.17 (s, 3H), 4.33 (s, 2H), 6.57 (s, 1H), 7.01 (d, J = 8.5 Hz, 1H), 7.67 (s, 2H), 8.15 (s, 1H), 8.46 (s, 1H)
Mass spectrometry value (ESI-MS, m/z): 483 (M⁺+1)

Example 429: 3-(Diethylamino)propyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0532] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-(diethylamino)-1-propanol (34 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (25 mg, yield 27%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.24 - 1.35 (m, 6H), 2.16 - 2.17 (m, 2H), 3.05 (brs, 6H), 4.07 (s, 6H), 4.28 (s, 2H), 7.19 (d, J = 8.5 Hz, 2H), 7.31 (s, 1H), 7.55 (s, 1H), 7.60 (d, J = 8.5 Hz, 2H), 8.22 (s, 1H), 8.60 (s, 1H)
Mass spectrometry value (ESI-MS, m/z): 456 (M⁺+1)

Example 430: 2-Pyridylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0533] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-pyridylmethanol (25 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (75 mg, yield 94%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.12 (s, 3H), 2.50 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 5.70 (s, 2H), 6.60 (s, 1H), 6.97 (s, 1H), 7.66 (s, 1H), 7.84 - 7.96 (m, 4H), 8.15 (s, 1H), 8.48 (s, 2H), 9.02 (s, 1H)
Mass spectrometry value (ESI-MS, m/z): 461 (M⁺+1)

Example 431: 2-Pyridylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0534] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-pyridylmethanol (25 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (50 mg, yield 63%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.10 (s, 3H), 2.47 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 5.70 (s, 2H), 6.59 (d, J = 5.9 Hz, 1H), 7.00 (d, J = 9.5 Hz, 1H), 7.68 (s, 2H), 7.75 - 7.97 (m, 3H), 8.15 (s, 1H), 8.48 (t, J = 7.1 Hz, 2H), 9.02 (d, J = 4.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 461 (M⁺+1)

Example 432: 3-Pyridylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0535] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-pyridylmethanol (25 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and

the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (80 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.12 (s, 3H), 2.33 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 5.47 (s, 2H), 6.58 (d, J = 6.8 Hz, 1H), 7.04 (d, J = 8.8 Hz, 1H), 7.67 (s, 2H), 7.98 - 8.01 (m, 1H), 8.14 (s, 1H), 8.46 (d, J = 8.1 Hz, 1H), 8.53 (s, 1H), 8.79 (d, J = 5.4 Hz, 1H), 9.22 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 461 (M⁺+1)

Example 433: 4-Pyridylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0536] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-pyridylmethanol (28 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (10 mg, yield 12%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 4.046 (s, 3H), 4.049 (s, 3H), 5.24 (s, 2H), 6.45 (d, J = 5.4 Hz, 1H), 7.17 (d, J = 8.8 Hz, 2H), 7.23 (s, 1H), 7.30 (d, J = 5.4 Hz, 2H), 7.45 (s, 1H), 7.53 (d, J = 8.3 Hz, 2H), 7.56 (s, 1H), 8.48 (d, J = 5.4 Hz, 1H), 8.62 (d, J = 5.4 Hz, 2H)

Mass spectrometry value (ESI-MS, m/z): 433 (M⁺+1)

Example 434: 4-Pyridylmethyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}carbamate

[0537] 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-pyridylmethanol (28 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (21 mg, yield 23%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 4.069 (s, 3H), 4.073 (s, 3H), 5.25 (s, 2H), 7.22 - 7.27 (m, 2H), 7.32 (d, J = 5.9 Hz, 2H), 7.34 (s, 1H), 7.53 (d, J = 8.8 Hz, 2H), 7.55 (s, 1H), 8.63 (d, J = 6.3 Hz, 3H)

Mass spectrometry value (ESI-MS, m/z): 433 (M⁺+1)

Example 435: 2-(Diethylamino)ethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0538] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-(diethylamino)-1-ethanol (31 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (53 mg, yield 61%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.08 (t, J = 7.1 Hz, 6H), 2.65 (q, J = 7.1 Hz, 4H), 2.79 (t, J = 5.9 Hz, 2H), 4.04 (s, 3H), 4.05 (s, 3H), 4.28 (t, J = 5.9 Hz, 2H), 6.44 (d, J = 5.4 Hz, 1H), 7.13 - 7.15 (m, 2H), 7.25 - 7.28 (m, 1H), 7.42 (s, 1H), 7.50 (d, J = 8.8 Hz, 2H), 7.56 (s, 1H), 8.48 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 441 (M⁺+1)

Example 436: 2-(Diethylamino)ethyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}carbamate

[0539] 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-(diethylamino)-1-ethanol (31 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium

bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (66 mg, yield 71%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.10 (t, J = 7.1 Hz, 6H), 2.67 (q, J = 7.1 Hz, 4H), 2.80 (t, J = 5.9 Hz, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 4.28 (t, J = 5.9 Hz, 2H), 7.10 (s, 1H), 7.19 - 7.21 (m, 2H), 7.32 (s, 1H), 7.51 (d, J = 8.8 Hz, 2H), 7.55 (s, 1H), 8.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 442 (M⁺+1)

Example 437: 1-(2-Morpholinoethyl)butyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0540] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-morpholino-3-hexanol (49 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (80 mg, yield 81%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.91 - 0.96 (m, 3H), 1.36 - 1.82 (m, 6H), 2.41 - 2.45 (m, 6H), 3.70 - 3.72 (m, 4H), 4.04 (s, 3H), 4.05 (s, 3H), 4.95 - 4.97 (m, 1H), 6.44 (d, J = 5.1 Hz, 1H), 7.14 (d, J = 8.8 Hz, 2H), 7.30 (s, 1H), 7.42 (s, 1H), 7.53 (d, J = 8.5 Hz, 2H), 7.57 (s, 1H), 8.47 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 511 (M⁺+1)

Example 438: 1-(2-Morpholinoethyl)butyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0541] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-morpholino-3-hexanol (43 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (74 mg, yield 81%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.96 (t, J = 7.3 Hz, 3H), 1.39 - 1.48 (m, 2H), 1.55 - 1.67 (m, 2H), 1.79 - 1.88 (m, 2H), 2.15 (s, 3H), 2.26 (s, 3H), 2.44 - 2.47 (m, 6H), 3.69 - 3.74 (m, 4H), 4.05 (s, 3H), 4.06 (s, 3H), 4.93 - 5.00 (m, 1H), 6.29 (d, J = 5.1 Hz, 1H), 6.51 (s, 1H), 6.93 (s, 1H), 7.29 (s, 1H), 7.42 (s, 1H), 7.60 (s, 1H), 7.79 (s, 1H), 8.44 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 539 (M⁺+1)

Example 439: 1-(2-Morpholinoethyl)butyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0542] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-morpholino-3-hexanol (43 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (82 mg, yield 90%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.96 (t, J = 7.3 Hz, 3H), 1.39 - 1.46 (m, 2H), 1.57 - 1.64 (m, 2H), 1.78 - 1.86 (m, 2H), 2.13 (s, 3H), 2.26 (s, 3H), 2.46 (s, 6H), 3.69 - 3.73 (m, 4H), 4.04 (s, 3H), 4.07 (s, 3H), 4.95 - 4.97 (m, 1H), 6.27 (d, J = 5.4 Hz, 1H), 6.75 (s, 1H), 7.00 (d, J = 8.5 Hz, 1H), 7.31 (s, 1H), 7.42 (s, 1H), 7.59 (s, 1H), 7.62 (s, 1H), 8.43 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 539 (M⁺+1)

Example 440: 1-(2-Morpholinoethyl)butyl N-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0543] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-morpholino-3-hexanol (49 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (77 mg, yield 73%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.84 - 0.88 (m, 3H), 1.28 - 1.75 (m, 6H), 2.34 - 2.37 (m, 6H), 3.63 - 3.65 (m, 4H), 3.98 (s, 3H), 3.99 (s, 3H), 4.86 - 4.87 (m, 1H), 7.00 (s, 1H), 7.12 (d, J = 8.8 Hz, 2H), 7.24 (s, 1H), 7.43 (d, J = 8.5 Hz, 2H), 7.48 (s, 1H), 8.54 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 512 (M⁺+1)

Example 441: 1-[2-(Diethylamino)ethyl]butyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]carbamate

[0544] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-(diethylamino)-3-hexanol (45 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (10 mg, yield 10%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.96 (t, J = 7.6 Hz, 3H), 1.28 (t, J = 7.6 Hz, 6H), 1.38 - 1.46 (m, 2H), 1.55 - 1.73 (m, 4H), 2.93 - 2.95 (m, 6H), 4.05 (s, 6H), 4.90 - 4.93 (m, 1H), 6.44 (d, J = 5.4 Hz, 1H), 7.14 (d, J = 9.0 Hz, 2H), 7.42 (s, 1H), 7.54 (d, J = 9.0 Hz, 2H), 7.56 (s, 1H), 8.47 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 497 (M⁺+1)

Example 442: 1-[2-(Diethylamino)ethyl]butyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0545] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-(diethylamino)-3-hexanol (40 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (29 mg, yield 32%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.96 (t, J = 7.3 Hz, 3H), 1.20 (t, J = 7.3 Hz, 6H), 1.37 - 1.49 (m, 2H), 1.55 - 1.71 (m, 2H), 1.93 - 1.98 (m, 2H), 2.15 (s, 3H), 2.26 (s, 3H), 2.76 - 2.80 (m, 6H), 4.05 (s, 3H), 4.06 (s, 3H), 4.89 - 4.96 (m, 1H), 6.29 (d, J = 5.4 Hz, 1H), 6.59 (s, 1H), 6.93 (s, 1H), 7.42 (s, 1H), 7.59 (s, 1H), 7.76 (s, 1H), 8.44 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 525 (M⁺+1)

Example 443: 1-[2-(Diethylamino)ethyl]butyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0546] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-(diethylamino)-3-hexanol (40 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (30 mg, yield 34%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.96 (t, J = 7.3 Hz, 3H), 1.19 (t, J = 6.6 Hz, 6H), 1.41 - 1.45 (m, 2H), 1.60 - 1.68 (m, 2H), 1.95 (brs, 2H), 2.12 (s, 3H), 2.26 (s, 3H), 2.78 - 2.80 (m, 6H), 4.05 (s, 3H), 4.07 (s, 3H), 4.92 (brs, 1H), 6.26 (d, J = 5.1 Hz, 1H), 6.65 (s, 1H), 6.99 (d, J = 8.5 Hz, 1H), 7.27 (s, 1H), 7.43 (s, 1H), 7.61 (s, 1H), 8.43 (d, J = 4.9

Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 525 (M⁺+1)

Example 444: 1-[2-(Diethylamino)ethyl]butyl N-[4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl]carbamate

[0547] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-(diethylamino)-3-hexanol (45 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (5 mg, yield 5%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.93 - 1.02 (m, 3H), 1.26 (t, J = 6.8 Hz, 6H), 1.37 - 1.45 (m, 2H), 1.54 - 2.03 (m, 4H), 2.90 (brs, 6H), 4.067 (s, 3H), 4.072 (s, 3H), 4.90 - 4.93 (m, 1H), 7.21 (d, J = 8.8 Hz, 2H), 7.32 (s, 1H), 7.49 - 7.56 (m, 3H), 8.61 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 498 (M⁺+1)

Example 445: 1-(2-Piperidinoethyl)butyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]carbamate

[0548] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-piperidino-3-hexanol (48 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (57 mg, yield 58%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.94 (t, J = 7.3 Hz, 3H), 1.35 - 1.46 (m, 4H), 1.52 - 1.67 (m, 6H), 1.85 - 1.90 (m, 2H), 2.40 - 2.56 (m, 6H), 4.04 (s, 3H), 4.05 (s, 3H), 4.90 - 4.93 (m, 1H), 6.44 (d, J = 5.4 Hz, 1H), 7.14 (d, J = 8.8 Hz, 2H), 7.28 (s, 3H), 7.42 (s, 1H), 7.52 (d, J = 8.8 Hz, 2H), 7.56 (s, 1H), 8.47 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 509 (M⁺+1)

Example 446: 1-(2-Piperidinoethyl)butyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0549] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-piperidino-3-hexanol (43 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (75 mg, yield 82%).

¹H-NMR (CDCl₃-d₁, 400 MHz) : δ 0.96 (t, J = 7.3 Hz, 3H), 1.38 - 1.46 (m, 4H), 1.57 - 1.67 (m, 6H), 1.84 - 1.89 (m, 2H), 2.15 (s, 3H), 2.25 (s, 3H), 2.43 - 2.47 (m, 6H), 4.05 (s, 3H), 4.06 (s, 3H), 4.89 - 4.95 (m, 1H), 6.29 (d, J = 5.1 Hz, 1H), 6.49 (s, 1H), 6.92 (s, 1H), 7.42 (s, 1H), 7.60 (s, 1H), 7.78 (s, 1H), 8.44 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 537 (M⁺+1)

Example 447: 1-(2-Piperidinoethyl)butyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0550] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-piperidino-3-hexanol (43 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (76 mg, yield 83%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.95 (t, J = 7.1 Hz, 3H), 1.46 (brs, 4H), 1.64 (brs, 6H), 1.87 - 1.88 (m, 2H), 2.04 (s, 3H), 2.12 (s, 3H), 2.26 (brs, 6H), 4.05 (s, 3H), 4.07 (s, 3H), 4.92 (brs, 1H), 6.26 (d, J = 4.9 Hz, 1H), 6.68 (s, 1H), 6.99 (d, J = 8.8 Hz, 1H), 7.42 (s, 1H), 7.62 (s, 2H), 8.43 (d, J = 4.9 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 537 (M⁺+1)

Example 448: 1-(2-Piperidinoethyl)butyl N-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0551] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-piperidino-3-hexanol (48 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (75 mg, yield 71%).

¹H-NMR (CDCl₃-d₁, 400 MHz) : δ 0.86 (t, J = 7.1 Hz, 3H), 1.30 - 1.33 (m, 4H), 1.39 - 1.57 (m, 6H), 1.77 - 1.80 (m, 2H), 2.34 - 2.41 (m, 6H), 3.99 (s, 3H), 4.00 (s, 3H), 4.82 - 4.83 (m, 1H), 7.12 (d, J = 8.5 Hz, 2H), 7.21 (s, 1H), 7.25 (s, 1H), 7.44 (d, J = 8.3 Hz, 2H), 7.48 (s, 1H), 8.54 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 510 (M⁺+1)

Example 449: 1-[2-(4-Methylpiperazino)ethyl]butyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]carbamate

[0552] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-(4-methylpiperazino)-3-hexanol (52 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (37 mg, yield 35%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.95 (t, J = 7.1 Hz, 3H), 1.37 - 1.44 (m, 2H), 1.56 - 1.65 (m, 2H), 1.78 - 1.83 (m, 2H), 2.30 (s, 3H), 2.44 - 2.48 (m, 10H), 4.047 (s, 3H), 4.050 (s, 3H), 4.93 - 4.94 (m, 1H), 6.43 (d, J = 5.4 Hz, 1H), 6.97 (s, 1H), 7.14 (d, J = 9.0 Hz, 2H), 7.42 (s, 1H), 7.50 (d, J = 8.5 Hz, 2H), 7.56 (s, 1H), 8.47 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 524 (M⁺+1)

Example 450: 1-[2-(4-Methylpiperazino)ethyl]butyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0553] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-(4-methylpiperazino)-3-hexanol (46 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (48 mg, yield 49%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.96 (t, J = 7.3 Hz, 3H), 1.39 - 1.46 (m, 2H), 1.58 - 1.64 (m, 2H), 1.82 - 1.85 (m, 2H), 2.15 (s, 3H), 2.25 (s, 3H), 2.31 (s, 3H), 2.48 - 2.50 (m, 10H), 4.05 (s, 3H), 4.07 (s, 3H), 6.29 (d, J = 5.1 Hz, 1H), 6.41 (s, 1H), 6.93 (s, 1H), 7.43 (s, 1H), 7.60 (s, 1H), 7.79 (s, 1H), 8.44 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 552 (M⁺+1)

Example 451: 1-[2-(4-Methylpiperazino)ethyl]butyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0554] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-(4-methylpiperazino)-3-hexanol (46 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated

aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (25 mg, yield 25%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.96 (t, J = 7.3 Hz, 3H), 1.40 - 1.45 (m, 2H), 1.57 - 1.63 (m, 2H), 1.82 - 1.84 (m, 2H), 2.12 (s, 3H), 2.25 (s, 3H), 2.31 (s, 3H), 2.46 - 2.49 (m, 10H), 4.05 (s, 3H), 4.07 (s, 3H), 4.94 (brs, 1H), 6.25 (d, J = 5.1 Hz, 1H), 6.45 (s, 1H), 6.99 (d, J = 8.8 Hz, 1H), 7.43 (s, 1H), 7.62 (s, 2H), 8.43 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 552 (M⁺+1)

Example 452: 1-[2-(4-Methylpiperazino)ethyl]butyl N-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]carbamate

[0555] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-(4-methylpiperazino)-3-hexanol (52 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (12 mg, yield 11%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.11 (t, J = 7.1 Hz, 3H), 1.37 - 1.42 (m, 2H), 1.53 - 1.60 (m, 2H), 1.70 - 1.80 (m, 2H), 2.21 (s, 3H), 2.31 - 2.50 (m, 10H), 4.07 (s, 6H), 4.94 (brs, 1H), 6.78 (s, 1H), 7.20 (d, J = 8.5 Hz, 1H), 7.32 (s, 1H), 7.50 (d, J = 8.5 Hz, 2H), 7.56 (s, 1H), 8.61 (s, 2H)

Mass spectrometry value (ESI-MS, m/z): 525 (M⁺+1)

Example 453: Cyano(phenyl)methyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]carbamate

[0556] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-hydroxy-2-phenylacetonitrile (35 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (20 mg, yield 24%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 4.04 (s, 3H), 4.06 (s, 3H), 5.95 (s, 1H), 6.58 (d, J = 5.1 Hz, 1H), 7.27 (s, 1H), 7.30 (d, J = 9.0 Hz, 2H), 7.46 - 7.58 (m, 8H), 8.54 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 457 (M⁺+1)

Example 454: Cyano(phenyl)methyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]carbamate

[0557] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-hydroxy-2-phenylacetonitrile (31 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (30 mg, yield 39%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.11 - 2.27 (m, 6H), 4.05 (s, 3H), 4.06 (s, 3H), 5.96 - 6.01 (m, 1H), 6.41 - 6.43 (m, 1H), 7.05 - 7.12 (m, 1H), 7.24 - 7.27 (m, 1H), 7.46 - 7.54 (m, 7H), 8.49 - 8.51 (m, 1H)

Mass spectrometry value (ESI-MS, m/z): 485 (M⁺+1)

Example 455: Cyano(phenyl)methyl N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]carbamate

[0558] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-hydroxy-2-phenylacetonitrile (31 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated

aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (30 mg, yield 39%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.10 - 2.26 (m, 6H), 4.06 (s, 6H), 5.98 - 6.02 (m, 1H), 6.36 - 6.38 (m, 1H), 7.08 - 7.12 (m, 1H), 7.20 - 7.27 (m, 1H), 7.46 - 7.57 (m, 7H), 8.47 - 8.49 (m, 1H)

Mass spectrometry value (ESI-MS, m/z): 485 (M⁺+1)

Example 456: 2-Cyanophenyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate

[0559] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-hydroxyphenyl cyanide (31 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (5 mg, yield 6%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 4.01 (s, 3H), 4.02 (s, 3H), 6.78 - 6.85 (m, 2H), 6.96 - 7.01 (m, 3H), 7.13 - 7.15 (m, 1H), 7.31 - 7.35 (m, 1H), 7.43 - 7.51 (m, 3H), 7.61 (s, 1H), 7.95 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 443 (M⁺+1)

Example 457: 3-Cyanophenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0560] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-hydroxybenzonitrile (31 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (5 mg, yield 6%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 4.11 (s, 3H), 4.19 (s, 3H), 6.78 (d, J = 5.6 Hz, 1H), 7.52 - 7.54 (m, 1H), 7.60 (s, 1H), 7.73 - 7.76 (m, 2H), 8.20 (s, 1H), 8.55 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 442 (M⁺+1)

Example 458: 3-Cyanophenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0561] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml) and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-hydroxybenzonitrile (27 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (40 mg, yield 53%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.13 - 2.16 (m, 3H), 2.28 - 2.39 (m, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 6.59 (d, J = 6.8 Hz, 1H), 7.03 (s, 1H), 7.15 - 7.19 (m, 2H), 7.52 - 7.57 (m, 3H), 7.65 (s, 1H), 8.12 - 8.13 (m, 1H), 8.45 - 8.47 (m, 1H)

Mass spectrometry value (ESI-MS, m/z): 471 (M⁺+1)

Example 459: 3-Cyanophenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0562] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml) and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 3-hydroxybenzonitrile (27 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order.

The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (40 mg, yield 53%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.10 - 2.15 (m, 3H), 2.27 - 2.37 (m, 3H), 4.11 (s, 3H), 4.16 (s, 3H), 6.56 (d, J = 6.6 Hz, 1H), 7.02 - 7.20 (m, 3H), 7.52 - 7.56 (m, 3H), 7.67 (s, 1H), 8.13 - 8.14 (m, 1H), 8.44 - 8.46 (m, 1H)

Mass spectrometry value (ESI-MS, m/z): 471 (M⁺+1)

Example 460: 4-Cyanophenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0563] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml) and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-hydroxybenzoxonitrile (27 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (40 mg, yield 53%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.16 (s, 3H), 2.39 (s, 3H), 4.11 (s, 3H), 4.17 (s, 3H), 6.97 (d, J = 8.3 Hz, 1H), 7.03 (s, 1H), 7.38 (d, J = 8.1 Hz, 2H), 7.65 (s, 1H), 7.74 (d, J = 8.3 Hz, 2H), 7.91 (brs, 1H), 8.15 (s, 1H), 8.49 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 471 (M⁺+1)

Example 461: 4-Cyanophenyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0564] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml) and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-hydroxybenzoxonitrile (27 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (40 mg, yield 53%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.10 - 2.14 (m, 3H), 2.27 - 2.37 (m, 3H), 4.11 - 4.17 (m, 6H), 6.56 (d, J = 6.1 Hz, 1H), 7.00 (d, J = 8.8 Hz, 2H), 7.38 (d, J = 8.8 Hz, 1H), 7.49 (d, J = 9.0 Hz, 2H), 7.67 (s, 1H), 7.73 (d, J = 8.8 Hz, 1H), 8.10 - 8.11 (m, 1H), 8.45 - 8.47 (m, 1H)

Mass spectrometry value (ESI-MS, m/z): 471 (M⁺+1)

Example 462: 1-Methyl-3-piperidyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0565] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml) and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-methyl-3-piperidinol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (23 mg, yield 27%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.69 - 1.88 (m, 6H), 2.37 (s, 3H), 2.54 - 2.57 (m, 1H), 2.72 (brs, 1H), 4.05 (s, 6H), 5.02 (s, 1H), 6.44 (d, J = 5.1 Hz, 1H), 7.14 (d, J = 8.8 Hz, 2H), 7.42 (s, 1H), 7.50 (d, J = 8.8 Hz, 2H), 7.56 (s, 1H), 8.47 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 439 (M⁺+1)

Example 463: 1-Methyl-3-piperidyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0566] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml) and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-methyl-3-piperidinol (27 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium

sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (29 mg, yield 36%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.77 (brs, 2H), 1.97 (brs, 2H), 2.14 (s, 3H), 2.25 (s, 3H), 2.35 (s, 3H), 2.60 - 2.67 (m, 4H), 4.05 (s, 3H), 4.06 (s, 3H), 5.01 (d, J = 4.1 Hz, 1H), 6.29 (d, J = 5.1 Hz, 1H), 6.69 (s, 1H), 6.91 (s, 1H), 7.42 (s, 1H), 7.59 (s, 1H), 7.82 (s, 1H), 8.44 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 467 (M⁺+1)

Example 464: 1-Methyl-3-piperidyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0567] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml) and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-methyl-3-piperidinol (27 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (22 mg, yield 27%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.69 - 1.90 (m, 6H), 2.11 (s, 3H), 2.26 (s, 3H), 2.37 (s, 3H), 2.62 (brs, 2H), 4.05 (s, 3H), 4.07 (s, 3H), 5.01 (s, 1H), 6.26 (d, J = 5.4 Hz, 1H), 6.99 (d, J = 8.8 Hz, 1H), 7.43 (s, 1H), 7.62 (s, 2H), 8.43 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 467 (M⁺+1)

Example 465: 1-Methyl-3-piperidyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)]phenyl}carbamate

[0568] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)]aniline (50 mg) was added to toluene (5 ml) and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-methyl-3-piperidinol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (26 mg, yield 28%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.69 - 1.96 (m, 6H), 2.37 (s, 3H), 2.57 - 2.70 (m, 2H), 4.066 (s, 3H), 4.071 (s, 3H), 5.01 (s, 1H), 7.20 (d, J = 8.8 Hz, 2H), 7.32 (s, 1H), 7.51 (d, J = 9.0 Hz, 2H), 7.56 (s, 1H), 8.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 440 (M⁺+1)

Example 466: 1-Methyl-4-piperidyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0569] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml) and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-methyl-4-piperidinol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (41 mg, yield 47%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.76 - 1.85 (m, 2H), 2.01 - 2.09 (m, 4H), 2.31 (s, 3H), 2.71 (brs, 2H), 4.05 (s, 6H), 4.82 (brs, 1H), 6.44 (d, J = 5.1 Hz, 1H), 6.89 (s, 1H), 7.15 (d, J = 8.8 Hz, 2H), 7.42 (s, 1H), 7.49 (d, J = 8.8 Hz, 2H), 7.56 (s, 1H), 8.48 (d, J = 5.1 Hz, 2H)

Mass spectrometry value (ESI-MS, m/z): 439 (M⁺+1)

Example 467: 1-Methyl-4-piperidyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0570] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml) and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-methyl-4-piperidinol (27 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (22 mg, yield 27%).

roform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (41 mg, yield 51%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.77 - 1.86 (m, 2H), 1.92 (brs, 2H), 2.03 - 2.05 (m, 2H), 2.16 (d, J = 9.0 Hz, 3H), 2.26 (s, 3H), 2.32 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), 4.80 - 4.82 (m, 1H), 6.29 (d, J = 5.4 Hz, 1H), 6.40 (s, 1H), 6.92 (s, 1H), 7.42 (s, 1H), 7.59 (s, 1H), 7.77 (brs, 1H), 8.44 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 467 (M⁺+1)

Example 468: 1-Methyl-4-piperidyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0571] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml) and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-methyl-4-piperidinol (27 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (33 mg, yield 41%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.76 - 1.85 (m, 2H), 2.01 (brs, 4H), 2.12 (s, 3H), 2.26 (s, 3H), 2.31 (s, 3H), 2.72 (brs, 2H), 4.05 (s, 3H), 4.07 (s, 3H), 4.78 - 4.82 (m, 1H), 6.26 (d, J = 5.4 Hz, 1H), 6.47 (s, 1H), 7.00 (d, J = 8.8 Hz, 1H), 7.43 (s, 1H), 7.62 (s, 2H), 8.44 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 467 (M⁺+1)

Example 469: 1-Methyl-4-piperidyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)]phenyl}carbamate

[0572] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)]aniline (50 mg) was added to toluene (5 ml) and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-methyl-4-piperidinol (30 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (33 mg, yield 37%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.78 - 1.85 (m, 4H), 2.01 (brs, 2H), 2.32 (s, 3H), 2.71 (brs, 2H), 4.067 (s, 3H), 4.071 (s, 3H), 4.81 (s, 1H), 6.74 (s, 1H), 7.21 (d, J = 9.0 Hz, 2H), 7.32 (s, 1H), 7.49 (d, J = 8.5 Hz, 2H), 7.55 (s, 1H), 8.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 440 (M⁺+1)

Example 470: Tetrahydro-2H-4-pyranyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}carbamate

[0573] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml) and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, tetrahydro-2H-4-pyranol (27 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (60 mg, yield 83%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.73 - 1.78 (m, 2H), 2.01 - 2.03 (m, 2H), 3.55 - 3.61 (m, 2H), 3.94 - 3.98 (m, 2H), 4.055 (s, 3H), 4.060 (s, 3H), 4.90 - 5.05 (m, 1H), 6.46 (d, J = 5.4 Hz, 1H), 6.67 (s, 1H), 7.16 (d, J = 8.8 Hz, 2H), 7.50 (d, J = 8.5 Hz, 2H), 7.56 (s, 1H), 8.48 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 426 (M⁺+1)

Example 471: Tetrahydro-2H-4-pyranyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}carbamate

[0574] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was added to toluene (5 ml) and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, tetrahydro-2H-4-pyranol

(24 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (57 mg, yield 84%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.75 - 1.79 (m, 2H), 1.98 - 2.10 (m, 2H), 2.15 (s, 3H), 2.27 (s, 3H), 3.55 - 3.61 (m, 2H), 3.96 - 3.99 (m, 2H), 4.07 (s, 6H), 4.90 - 5.00 (m, 1H), 6.31 (d, J = 4.9 Hz, 1H), 6.37 (s, 1H), 6.93 (s, 1H), 7.49 (s, 1H), 7.60 (s, 1H), 7.78 (s, 1H), 8.45 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 454 (M⁺+1)

Example 472: Tetrahydro-2H-4-pyranyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}carbamate

[0575] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml) and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (68 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, tetrahydro-2H-4-pyranol (24 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (23 mg, yield 34%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.72 - 1.81 (m, 2H), 2.01 - 2.06 (m, 2H), 2.13 (s, 3H), 2.26 (s, 3H), 3.55 - 3.60 (m, 2H), 3.94 - 3.99 (m, 2H), 4.071 (s, 3H), 4.073 (s, 3H), 4.95 - 5.00 (m, 1H), 6.30 (d, J = 5.4 Hz, 1H), 6.40 (s, 1H), 7.01 (d, J = 8.8 Hz, 1H), 7.52 (s, 1H), 7.62 (s, 1H), 8.44 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 454 (M⁺+1)

Example 473: Tetrahydro-2H-4-pyranyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate

[0576] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (50 mg) was added to toluene (5 ml) and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (77 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, tetrahydro-2H-4-pyranol (27 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (38 mg, yield 53%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.70 - 1.80 (m, 2H), 2.00 - 2.05 (m, 2H), 3.55 - 3.60 (m, 2H), 3.94 - 3.98 (m, 2H), 4.07 (s, 6H), 4.93 - 5.01 (m, 1H), 6.65 (s, 1H), 7.22 (d, J = 8.8 Hz, 2H), 7.35 (s, 1H), 7.51 (d, J = 10.5 Hz, 2H), 7.56 (s, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 426 (M⁺+1)

Example 474: Cyclohexyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]-N-methylcarbamate

[0577] Dimethylformamide (5 ml) was added to sodium hydride (12 mg), and cyclohexyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate (70 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of methyl iodide (43 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (70 mg, yield 99%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.23 - 1.92 (m, 10H), 3.26 (s, 3H), 4.07 (s, 3H), 4.08 (s, 3H), 4.73 (s, 1H), 7.21 - 7.23 (m, 1H), 7.27 (s, 1H), 7.34 (s, 1H), 7.41 (d, J = 2.7 Hz, 1H), 7.52 (s, 1H), 8.65 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 473 (M⁺+1)

Example 475: Cyclohexyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]-N-ethylcarbamate

[0578] Dimethylformamide (5 ml) was added to sodium hydride (11 mg), and cyclohexyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]carbamate (65 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of ethyl iodide (87 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by

washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (60 mg, yield 88%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.20 (t, J = 6.8 Hz, 3H), 1.24 - 1.91 (m, 10H), 3.54 - 3.59 (m, 1H), 3.83 - 3.89 (m, 1H), 4.07 (s, 3H), 4.08 (s, 3H), 4.73 (brs, 1H), 7.21 - 7.24 (m, 2H), 7.34 (s, 1H), 7.43 (d, J = 2.7 Hz, 1H), 7.52 (s, 1H), 8.65 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 487 (M⁺+1)

Example 476: Cyclohexyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N-methylcarbamate

[0579] Dimethylformamide (5 ml) was added to sodium hydride (7 mg), and cyclohexyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate (35 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of methyl iodide (47 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (30 mg, yield 83%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.26 - 1.83 (m, 10H), 3.35 (s, 3H), 4.07 (s, 6H), 4.75 - 4.79 (m, 1H), 7.24 (d, J = 8.8 Hz, 2H), 7.34 - 7.35 (m, 3H), 7.56 (s, 1H), 8.65 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 439 (M⁺+1)

Example 477: Cyclohexyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N-ethylcarbamate

[0580] Dimethylformamide (5 ml) was added to sodium hydride (7 mg), and cyclohexyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate (35 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of ethyl iodide (52 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (35 mg, yield 93%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.23 (t, J = 7.1 Hz, 3H), 1.36 - 1.93 (m, 10H), 3.73 - 3.78 (m, 1H), 3.91 - 3.98 (m, 1H), 4.07 (s, 6H), 4.76 (s, 1H), 7.19 - 7.34 (m, 4H), 7.51 (d, J = 11.0 Hz, 1H), 7.56 (s, 1H), 8.64 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 453 (M⁺+1)

Example 478: 2-Methoxybenzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N-methylcarbamate

[0581] Dimethylformamide (5 ml) was added to sodium hydride (11 mg), and 2-methoxybenzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate (66 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of methyl iodide (77 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (50 mg, yield 75%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.29 (s, 3H), 3.87 (s, 3H), 4.065 (s, 3H), 4.07 (s, 3H), 4.69 (s, 2H), 6.83 - 6.96 (m, 4H), 7.20 - 7.50 (m, 5H), 8.64 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 511 (M⁺+1)

Example 479: 2-Methylbenzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N-methylcarbamate

[0582] Dimethylformamide (5 ml) was added to sodium hydride (11 mg), and 2-methylbenzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate (62 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of methyl iodide (77 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (57 mg, yield 89%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.21 (s, 3H), 3.28 (s, 3H), 4.069 (s, 3H), 4.074 (s, 3H), 5.10 - 5.19 (m, 2H), 7.12 - 7.23 (m, 5H), 7.33 - 7.35 (m, 2H), 7.41 (d, J = 2.4 Hz, 1H), 7.51 (s, 1H), 8.64 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 495 (M⁺+1)

Example 480: 2-Chlorobenzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N-methylcarbamate

[0583] Dimethylformamide (5 ml) was added to sodium hydride (11 mg), and 2-chlorobenzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate (65 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of methyl iodide (77 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (57 mg, yield 85%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.30 (s, 3H), 4.07 (s, 3H), 4.08 (s, 3H), 5.20 - 5.27 (m, 2H), 7.20 - 7.27 (m, 4H), 7.34 - 7.44 (m, 4H), 7.51 (s, 1H), 8.65 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 515 (M⁺+1)

Example 481: 1-Propylbutyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N-methylcarbamate

[0584] Dimethylformamide (5 ml) was added to sodium hydride (11 mg), and 1-propylbutyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate (62 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of methyl iodide (77 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (43 mg, yield 68%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.87 (t, J = 7.1 Hz, 6H), 1.24 - 1.82 (s, 8H), 3.26 (s, 3H), 4.07 (s, 3H), 4.08 (s, 3H), 4.80 - 4.83 (m, 1H), 7.21 - 7.24 (m, 1H), 7.31 (s, 1H), 7.34 (s, 1H), 7.42 (s, 1H), 7.52 (s, 1H), 8.66 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 489 (M⁺+1)

Example 482: Cycloheptyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N-methylcarbamate

[0585] Dimethylformamide (5 ml) was added to sodium hydride (11 mg), and cycloheptyl N-2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenylcarbamate (61 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of methyl iodide (77 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (60 mg, yield 95%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.44 - 1.93 (m, 12H), 3.25 (s, 3H), 4.07 (s, 3H), 4.08 (s, 3H), 4.90 (brs, 1H), 7.20 - 7.23 (m, 1H), 7.33 - 7.34 (m, 2H), 7.41 (d, J = 2.7 Hz, 1H), 7.52 (s, 1H), 8.65 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 487 (M⁺+1)

Example 483: Cycloheptylmethyl N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N-methylcarbamate

[0586] Dimethylformamide (5 ml) was added to sodium hydride (27 mg), and cycloheptylmethyl N-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenylcarbamate (153 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of methyl iodide (193 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (100 mg, yield 63%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.15 - 1.81 (m, 13H), 3.42 (d, J = 6.6 Hz, 3H), 3.99 (d, J = 6.6 Hz, 2H), 4.05 (s, 6H), 6.44 (d, J = 5.4 Hz, 1H), 7.14 (d, J = 9.0 Hz, 2H), 7.43 (s, 1H), 7.49 (d, J = 8.5 Hz, 2H), 7.56 (s, 1H), 8.48 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 466 (M⁺+1)

Example 484: Cycloheptylmethyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N-methylcarbamate

[0587] Dimethylformamide (5 ml) was added to sodium hydride (27 mg), and cycloheptylmethyl N-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenylcarbamate (154 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of methyl iodide (193 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (90 mg, yield 57%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.10 - 1.81 (m, 13H), 3.35 (s, 3H), 3.94 (d, J = 6.6 Hz, 2H), 4.07 (s, 6H), 7.23 - 7.26 (m, 3H), 7.34 - 7.35 (m, 2H), 7.56 (s, 1H), 8.64 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 467 (M⁺+1)

5 Example 485: 2-Methoxybenzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N-ethylcarbamate

[0588] Dimethylformamide (5 ml) was added to sodium hydride (11 mg), and 2-methoxybenzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate (66 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of ethyl iodide (84 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (63 mg, yield 93%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.22 (t, J = 7.1 Hz, 3H), 3.55 - 3.60 (m, 1H), 3.76 - 3.94 (m, 1H), 3.87 (s, 3H), 4.067 (s, 3H), 4.074 (s, 3H), 5.19 (d, J = 3.4 Hz, 2H), 6.81 - 7.09 (m, 4H), 7.21 - 7.40 (m, 3H), 7.43 (d, J = 2.7 Hz, 1H), 7.51 (s, 1H), 8.65 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 525 (M⁺+1)

20 Example 486: 2-Methylbenzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N-ethylcarbamate

[0589] Dimethylformamide (5 ml) was added to sodium hydride (11 mg), and 2-methylbenzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate (62 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of ethyl iodide (84 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (53 mg, yield 79%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.20 - 1.23 (m, 3H), 2.21 (s, 3H), 3.56 - 3.59 (m, 1H), 3.90 - 3.92 (m, 1H), 4.069 (s, 3H), 4.073 (s, 3H), 5.13 - 5.18 (m, 1H), 7.12 - 7.36 (m, 7H), 7.43 (s, 1H), 7.51 (s, 1H), 8.64 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 509 (M⁺+1)

30 Example 487: 2-Chlorobenzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N-ethylcarbamate

[0590] Dimethylformamide (5 ml) was added to sodium hydride (11 mg), and 2-chlorobenzyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate (65 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of ethyl iodide (84 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (68 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.23 (t, J = 7.1 Hz, 3H), 3.54 - 3.63 (m, 1H), 3.88 - 3.97 (m, 1H), 4.07 (s, 3H), 4.08 (s, 3H), 5.23 (s, 2H), 7.19 - 7.36 (m, 7H), 7.45 (d, J = 2.4 Hz, 1H), 7.51 (s, 1H), 8.65 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 529 (M⁺+1)

45 Example 488: 1-Propylbutyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N-ethylcarbamate

[0591] Dimethylformamide (5 ml) was added to sodium hydride (11 mg), and 1-propylbutyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}carbamate (62 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of ethyl iodide (84 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (49 mg, yield 75%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.85 - 0.88 (m, 3H), 0.93 - 0.97 (s, 3H), 1.18 - 1.70 (m, 11H), 3.47 - 3.53 (m, 1H), 3.88 - 3.91 (m, 1H), 4.07 (s, 3H), 4.08 (s, 3H), 4.78 - 4.95 (m, 1H), 7.21 - 7.23 (m, 1H), 7.32 - 7.34 (m, 2H), 7.43 (s, 1H), 7.52 (s, 1H), 8.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 503 (M⁺+1)

Example 489: Cycloheptyl N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N-ethylcarbamate

[0592] Dimethylformamide (5 ml) was added to sodium hydride (11 mg), and cycloheptyl N-2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenylcarbamate (61 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of ethyl iodide (84 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (51 mg, yield 78%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.20 (t, J = 7.1 Hz, 3H), 1.29 - 2.03 (m, 12H), 3.53 - 3.58 (m, 1H), 3.83 - 3.88 (m, 1H), 4.07 (s, 3H), 4.08 (s, 3H), 4.89 - 4.98 (m, 1H), 7.21 - 7.23 (m, 1H), 7.27 - 7.34 (m, 2H), 7.43 (d, J = 2.7 Hz, 1H), 7.52 (s, 1H), 8.65 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 501 (M⁺+1)

Example 490: 2-Methoxybenzyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N-methylcarbamate

[0593] Dimethylformamide (5 ml) was added to sodium hydride (24 mg), and 2-methoxybenzyl N-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenylcarbamate (145 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of methyl iodide (170 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (115 mg, yield 81%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.38 (s, 3H), 3.84 (s, 3H), 4.06 (s, 6H), 5.24 (s, 2H), 6.86 - 6.93 (m, 3H), 7.23 - 7.28 (m, 3H), 7.33 (s, 1H), 7.38 (d, J = 8.8 Hz, 2H), 7.54 (s, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 477 (M⁺+1)

Example 491: 2-Methylbenzyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N-methylcarbamate

[0594] Dimethylformamide (5 ml) was added to sodium hydride (24 mg), and 2-methylbenzyl N-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenylcarbamate (148 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of methyl iodide (170 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (115 mg, yield 83%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.32 (s, 3H), 3.37 (s, 3H), 4.07 (s, 6H), 5.20 (s, 2H), 7.16 - 7.27 (m, 6H), 7.33 (s, 1H), 7.36 (d, J = 6.6 Hz, 2H), 7.55 (s, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 461 (M⁺+1)

Example 492: 2-Chlorobenzyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N-methylcarbamate

[0595] Dimethylformamide (5 ml) was added to sodium hydride (16 mg), and 2-chlorobenzyl N-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenylcarbamate (107 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of methyl iodide (114 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (75 mg, yield 78%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.39 (s, 3H), 4.07 (s, 6H), 5.29 (s, 2H), 7.24 - 7.41 (m, 9H), 7.55 (s, 1H), 8.64 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 481 (M⁺+1)

Example 493: 1-Propylbutyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N-methylcarbamate

[0596] Dimethylformamide (5 ml) was added to sodium hydride (16 mg), and 1-propylbutyl N-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenylcarbamate (99 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of methyl iodide (114 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (84 mg, yield 93%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.92 (t, J = 7.3 Hz, 6H), 1.18 - 1.42 (m, 4H), 1.45 - 1.55 (m, 4H), 3.35 (s, 3H),

4.07 (s, 6H), 4.83 - 4.89 (m, 1H), 7.25 (d, J = 8.8 Hz, 2H), 7.33 (s, 1H), 7.36 (d, J = 8.5 Hz, 2H), 7.55 (s, 1H), 8.64 (s, 1H)
Mass spectrometry value (ESI-MS, m/z): 455 (M⁺+1)

Example 494: Cycloheptyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}-N-methylcarbamate

[0597] Dimethylformamide (5 ml) was added to sodium hydride (24 mg), and cycloheptyl N-4-[(6,7-dimethoxy-4-quinazolinyloxy]phenylcarbamate (144 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of methyl iodide (170 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (117 mg, yield 86%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.26 - 1.93 (m, 12H), 3.34 (s, 3H), 4.07 (s, 6H), 4.91 - 4.95 (m, 1H), 7.24 (d, J = 8.8 Hz, 2H), 7.33 (s, 1H), 7.36 (d, J = 8.8 Hz, 2H), 7.55 (s, 1H), 8.64 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 453 (M⁺+1)

Example 495: 1-Ethyl-3-butynyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}-N-methylcarbamate

[0598] Dimethylformamide (5 ml) was added to sodium hydride (27 mg), and 1-ethyl-3-butynyl N-4-[(6,7-dimethoxy-4-quinazolinyloxy]phenylcarbamate (143 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of methyl iodide (193 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (83 mg, yield 56%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.84 (t, J = 7.6 Hz, 3H), 1.64 - 1.65 (m, 2H), 1.93 (t, J = 2.7 Hz, 2H), 2.44 (brs, 2H), 3.28 (s, 3H), 3.99 (s, 3H), 4.75 - 4.78 (m, 1H), 7.17 (d, J = 8.8 Hz, 2H), 7.21 (s, 1H), 7.31 (d, J = 8.8 Hz, 2H), 7.47 (s, 1H), 8.56 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 437 (M⁺+1)

Example 496: 1-Ethyl-3-butynyl N-{4-[(6,7-dimethoxy-4-quinolinyloxy]phenyl}-N-methylcarbamate

[0599] Dimethylformamide (5 ml) was added to sodium hydride (27 mg), and 1-ethyl-3-butynyl N-4-[(6,7-dimethoxy-4-quinolinyloxy]phenylcarbamate (143 mg) was added to the mixture. Subsequently, a dimethylformamide solution (2 ml) of methyl iodide (193 mg) was added thereto, and the mixture was stirred at room temperature for 10 min. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (24 mg, yield 16%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.85 - 0.87 (m, 3H), 1.67 - 1.75 (m, 2H), 1.918 - 1.924 (m, 1H), 2.46 (s, 2H), 3.29 (s, 3H), 3.97 (s, 3H), 3.98 (s, 3H), 4.76 - 4.79 (m, 1H), 6.44 (d, J = 5.4 Hz, 1H), 7.09 (d, J = 9.0 Hz, 2H), 7.30 (d, J = 8.5 Hz, 2H), 7.36 (s, 1H), 7.47 (s, 1H), 8.43 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 436 (M⁺+1)

Example 497: Cyclohexyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy]-2-methoxyphenyl}carbamate

[0600] 4-[(6,7-Dimethoxy-4-quinazolinyloxy]-2-methoxyaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cyclohexanol (47 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (120 mg, yield 85%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.26 - 1.95 (m, 10H), 3.88 (s, 3H), 4.07 (s, 6H), 4.68 - 4.77 (m, 1H), 6.79 - 6.80 (m, 1H), 6.84 - 6.87 (m, 1H), 7.17 (s, 1H), 7.32 (s, 1H), 7.55 (s, 1H), 8.19 (s, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 455 (M⁺+1)

Example 498: Cycloheptyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy]-2-methoxyphenyl}carbamate

[0601] 4-[(6,7-Dimethoxy-4-quinazolinyloxy]-2-methoxyaniline (100 mg) was added to toluene (10 ml) and triethyl-

amine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cycloheptanol (54 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (89 mg, yield 61%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.49 - 2.03 (m, 13H), 3.88 (s, 3H), 4.07 (s, 6H), 4.84 - 4.97 (m, 1H), 6.788 - 6.794 (m, 1H), 6.84 - 6.87 (m, 1H), 7.15 (s, 1H), 7.36 (s, 1H), 7.55 (s, 1H), 8.19 (s, 1H), 8.64 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 469 (M⁺+1)

Example 499: 2-Chlorobenzyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-methoxyphenyl}carbamate

[0602] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-methoxyaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-chlorophenyl) methanol (67 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (147 mg, yield 96%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.86 (s, 3H), 4.06 (s, 3H), 4.07 (s, 3H), 5.34 (s, 2H), 6.80 - 6.81 (m, 1H), 6.85 - 6.88 (m, 1H), 7.27 - 7.35 (m, 4H), 7.40 - 7.42 (m, 1H), 7.48 - 7.51 (m, 1H), 7.55 (s, 1H), 8.21 (s, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 497 (M⁺+1)

Example 500: 2-Methoxybenzyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-methoxyphenyl}carbamate

[0603] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-methoxyaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-methoxyphenyl)methanol (58 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (148 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.86 - 3.91 (m, 8H), 4.06 (s, 3H), 4.07 (s, 3H), 6.84 - 7.32 (m, 6H), 7.33 (s, 1H), 7.55 (s, 1H), 8.23 - 8.30 (m, 1H), 8.65 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 493 (M⁺+1)

Example 501: 2-(2-Pyridyl)ethyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-methoxyphenyl}carbamate

[0604] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-methoxyaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 2-(2-pyridyl)-1-ethanol (58 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, and the extract was washed with water and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (110 mg, yield 75%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.20 (t, J = 6.8 Hz, 2H), 3.85 (d, J = 1.5 Hz, 3H), 4.07 (d, J = 1.5 Hz, 6H), 4.60 (t, J = 6.6 Hz, 2H), 6.78 - 6.89 (m, 1H), 6.84 (d, J = 8.8 Hz, 1H), 7.16 - 7.27 (m, 3H), 7.32 (d, J = 1.5 Hz, 1H), 7.54 (d, J = 1.5 Hz, 1H), 7.62 - 7.66 (m, 1H), 8.18 (brs, 1H), 8.58 (d, J = 4.9 Hz, 1H), 8.63 (d, J = 1.7 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 478 (M⁺+1)

Example 502: 1-Ethyl-3-butenyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-methoxyphenyl}carbamate

[0605] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-methoxyaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in

methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 5-hexyn-3-ol (46 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (73 mg, yield 52%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.00 (t, J = 7.3 Hz, 3H), 1.74 - 1.85 (m, 2H), 2.56 - 2.59 (m, 1H), 3.31 - 3.49 (m, 2H), 3.89 (s, 3H), 4.07 (s, 6H), 4.89 - 4.92 (m, 1H), 6.80 (d, J = 2.4 Hz, 1H), 6.85 - 6.87 (m, 1H), 7.27 (s, 1H), 7.33 (s, 1H), 7.55 (s, 1H), 8.20 (brs, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 453 (M⁺+1)

Example 503: Cyclohexyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}carbamate

[0606] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-nitroaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cyclohexanol (44 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (120 mg, yield 88%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.24 - 1.57 (m, 6H), 1.78 - 1.81 (m, 2H), 1.96 - 2.04 (m, 2H), 4.07 (s, 6H), 4.78 - 4.82 (m, 1H), 7.34 (s, 1H), 7.52 (s, 1H), 7.58 - 7.61 (m, 1H), 8.17 (d, J = 2.9 Hz, 1H), 8.61 (s, 1H), 8.73 (d, J = 9.3 Hz, 1H), 9.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 470 (M⁺+1)

Example 504: 2-Chlorobenzyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}carbamate

[0607] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-nitroaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-chlorophenyl)methanol (63 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (74 mg, yield 50%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 4.08 (s, 6H), 5.39 (s, 2H), 7.26 - 7.33 (m, 2H), 7.37 (s, 1H), 7.43 - 7.45 (m, 1H), 7.49 - 7.52 (m, 2H), 7.59 - 7.62 (m, 1H), 8.18 (d, J = 2.7 Hz, 1H), 8.61 (s, 1H), 8.74 (d, J = 9.3 Hz, 1H), 9.97 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 512 (M⁺+1)

Example 505: 2-Methylbenzyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}carbamate

[0608] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-nitroaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, (2-methylphenyl)methanol (54 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (130 mg, yield 91%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.42 (s, 3H), 4.06 (s, 3H), 4.07 (s, 3H), 5.29 (s, 2H), 7.17 - 7.41 (m, 5H), 7.51 (s, 1H), 7.58 - 7.61 (m, 1H), 8.16 (d, J = 2.9 Hz, 1H), 8.59 (s, 1H), 8.73 (d, J = 9.3 Hz, 1H), 9.90 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

Example 506: Cycloheptylmethyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}carbamate

[0609] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-nitroaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene

chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, cycloheptylmethanol (56 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (115 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.23 - 1.93 (m, 13H), 4.03 (d, J = 6.8 Hz, 2H), 4.077 (s, 3H), 4.081 (s, 3H), 7.27 (s, 1H), 7.34 (s, 1H), 7.52 (s, 1H), 7.58 - 7.61 (m, 1H), 8.17 (d, J = 2.7 Hz, 1H), 8.61 (s, 1H), 8.73 (d, J = 9.3 Hz, 1H), 9.85 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 498 (M⁺+1)

Example 507: Cycloheptyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}carbamate

[0610] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-nitroaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-cycloheptanol (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (140 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.40 - 1.82 (m, 8H), 1.88 - 1.94 (m, 2H), 1.98 - 2.04 (m, 2H), 4.077 (s, 3H), 4.080 (s, 3H), 4.95 - 5.00 (m, 1H), 7.35 (s, 1H), 7.52 (s, 1H), 7.57 - 7.60 (m, 1H), 8.16 (d, J = 2.7 Hz, 1H), 8.61 (s, 1H), 8.74 (d, J = 9.3 Hz, 1H), 9.79 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 484 (M⁺+1)

Example 508: 1-Butylpentyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}carbamate

[0611] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-nitroaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 5-nonanol (64 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (143 mg, yield 96%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.89 - 0.94 (m, 6H), 1.33 - 1.65 (m, 12H), 4.077 (s, 3H), 4.083 (s, 3H), 4.89 - 4.92 (m, 1H), 7.35 (s, 1H), 7.52 (s, 1H), 7.57 - 7.60 (m, 1H), 8.17 (d, J = 2.7 Hz, 1H), 8.60 (s, 1H), 8.76 (d, J = 9.3 Hz, 1H), 9.83 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 514 (M⁺+1)

Example 509: Hexyl N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}carbamate

[0612] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-nitroaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-hexanol (45 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (109 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.92 (t, J = 7.1 Hz, 3H), 1.34 - 1.42 (m, 6H), 1.69 - 1.76 (m, 2H), 4.079 (s, 3H), 4.082 (s, 3H), 4.23 (t, J = 6.8 Hz, 2H), 7.35 (s, 1H), 7.52 (s, 1H), 7.58 - 7.61 (m, 1H), 8.17 (d, J = 2.9 Hz, 1H), 8.61 (s, 1H), 8.73 (d, J = 9.3 Hz, 1H), 9.85 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 472 (M⁺+1)

Example 510: 1-Ethyl-3-butynyl N-{4-[(6,7-dimethoxy-4-quinazolinyloxy)-2-nitrophenyl]carbamate

[0613] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-nitroaniline (100 mg) was added to toluene (10 ml) and triethylamine (1 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (140 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 5-hexyn-3-ol (43 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with a 1 N aqueous hydrochloric acid solution, water, and saturated brine in that order. The extract was dried over sodium sulfate and was then concentrated. The residue was purified on a column using chloroform/methanol to give the title compound (115 mg, yield 85%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.01 (t, J = 7.3 Hz, 3H), 1.77 - 1.87 (m, 2H), 2.04 - 2.05 (m, 1H), 2.58 - 2.60 (m, 2H), 4.079 (s, 3H), 4.083 (s, 3H), 4.91 - 4.96 (m, 1H), 7.35 (s, 1H), 7.52 (s, 1H), 7.59 - 7.62 (m, 1H), 8.18 (d, J = 2.7 Hz, 1H), 8.61 (s, 1H), 8.73 (d, J = 9.3 Hz, 1H), 9.87 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 467 (M⁺+1)

Example 511: N-{4-[(6,7-Dimethoxy-4-quinolyloxy)-2,3-dimethylphenyl]-N'-(2-diethylaminoethyl)thiourea

[0614] 4-[(6,7-Dimethoxy-4-quinolyloxy)-2,3-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, N,N-diethylphenylenediamine (50 mg) was added to thereto, and the mixture was further stirred at room temperature for 14 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (5 mg, yield 5%).

¹H-NMR (CDCl₃, 400 MHz): 0.89 (m, 6H), 2.15 (s, 3H), 2.28 (s, 3H), 2.46 (m, 4H), 2.62 (m, 2H), 3.67 (m, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 6.25 (m, 1H), 6.76 (br, 1H), 7.04 (d, J = 8.5 Hz, 1H), 7.18 (d, J = 8.6 Hz, 1H), 7.44 (s, 1H), 7.46 (br, 1H), 7.59 (s, 1H), 8.44 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 483 (M⁺+1)

Example 512: N-{4-[(6,7-Dimethoxy-4-quinolyloxy)-2,3-dimethylphenyl]-N'-(2-piperidinyloethyl)thiourea

[0615] 4-[(6,7-Dimethoxy-4-quinolyloxy)-2,3-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 3 hr. Next, 2-piperidinyloethylamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 16 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (25 mg, yield 33%).

¹H-NMR (CDCl₃, 400 MHz): 1.35 - 1.46 (m, 6H), 2.17 (s, 3H), 2.29 (s, 3H), 2.32 - 2.56 (m, 6H), 3.69 (m, 2H), 4.06 (s, 6H), 6.29 (m, 1H), 6.78 (br, 1H), 7.05 (d, J = 8.3 Hz, 1H), 7.19 (d, J = 8.6 Hz, 1H), 7.48 (s, 1H), 7.50 (br, 1H), 7.59 (s, 1H), 8.45 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 494 (M⁺+1)

Example 513: N-{4-[(6,7-Dimethoxy-4-quinolyloxy)-2,3-dimethylphenyl]-N'-[4-(N-benzyl)piperidinyl]thiourea

[0616] 4-[(6,7-Dimethoxy-4-quinolyloxy)-2,3-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 3 hr. Next, 4-amino-1-benzylpiperidine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 16 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (27 mg, yield 31%).

¹H-NMR (CDCl₃, 400 MHz): 1.38 - 2.26 (m, 10H), 2.80 - 2.88 (m, 4H), 3.53 (m, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 5.46 (br, 1H), 6.28 (d, J = 5.4 Hz, 1H), 7.03 (d, J = 8.3 Hz, 1H), 7.14 (d, J = 8.5 Hz, 1H), 7.28 - 7.33 (m, 5H), 7.45 (s, 1H), 7.47 (br, 1H), 7.58 (s, 1H), 8.49 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 556 (M⁺+1)

Example 514: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}-N'-(2-piperidinyloxy)thiourea

[0617] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (52 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 5 hr. Next, 2-piperidinyloxyamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 15 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (32 mg, yield 40%).

¹H-NMR (CDCl₃, 400 MHz): 1.35 - 1.46 (m, 6H), 2.17 (s, 3H), 2.29 (s, 3H), 2.32 - 2.56 (m, 6H), 3.69 (m, 2H), 4.06 (s, 6H), 6.29 (m, 1H), 6.78 (br, 1H), 7.05 (d, J = 8.3 Hz, 1H), 7.19 (d, J = 8.6 Hz, 1H), 7.48 (s, 1H), 7.50 (br, 1H), 7.59 (s, 1H), 8.45 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 494 (M⁺+1)

Example 515: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}-N'-(2-acetamidoethyl)thiourea

[0618] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (52 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 5 hr. Next, 2-acetamidoethylamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 15 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (6 mg, yield 8%).

¹H-NMR (CDCl₃, 400 MHz): 1.94 (s, 3H), 2.17 (s, 3H), 2.25 (s, 3H), 3.44 (m, 2H), 3.78 (m, 2H), 4.07 (s, 6H), 6.20 (m, 1H), 6.67 (br, 1H), 6.78 (br, 1H), 7.07 (s, 1H), 7.18 (s, 1H), 7.41 (br, 1H), 7.54 (s, 1H), 7.59 (s, 1H), 8.47 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 468 (M⁺+1)

Example 516: N-{4-[(6,7-Dimethoxy-4-quinazolinyloxy)phenyl]-N'-(2-diethylaminoethyl)thiourea

[0619] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (50 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 5 hr. Next, N,N-diethylethylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 15 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (62 mg, yield 81%).

¹H-NMR (CDCl₃, 400 MHz): 0.96 (br, 6H), 2.52 (br, 4H), 2.67 (br, 2H), 3.68 (br, 2H), 4.07 (s, 6H), 7.26 - 7.54 (m, 7H), 7.83 (br, 1H), 8.59 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 456 (M⁺+1)

Example 517: N-{4-[(6,7-Dimethoxy-4-quinazolinyloxy)phenyl]-N'-[2-(1-piperidinyloxy)ethyl]thiourea

[0620] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (50 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, 2-(1-piperidinyloxy)ethylamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 14 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (35 mg, yield 45%).

¹H-NMR (CDCl₃, 400 MHz): 1.40 - 1.55 (m, 6H), 2.40 - 2.60 (m, 6H), 3.72 (m, 2H), 4.07 (s, 6H), 7.30 - 7.38 (m, 7H), 7.54 (s, 1H), 8.60 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 468 (M⁺+1)

Example 518: N-{4-[(6,7-Dimethoxy-4-quinazolinyloxy)phenyl]-N'-[4-(1-benzylpiperidinyloxy)]thiourea

[0621] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (50 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was

stirred at room temperature for 6 hr. Next, 4-amino-1-benzylpiperidine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 14 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (40 mg, yield 44%).

¹H-NMR (CDCl₃, 400 MHz): 1.52 (m, 2H), 2.09 (m, 2H), 2.19 (m, 2H), 2.83 (m, 2H), 3.52 (s, 2H), 4.08 (s, 6H), 4.37 (m, 1H), 6.06 (d, J = 7.8 Hz, 1H), 7.28 - 7.35 (m, 10H), 7.53 (s, 1H), 7.80 (br, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 530 (M⁺+1)

Example 519: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(2-acetamidomethyl)thiourea

[0622] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, N-acetylenehydrazine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 14 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (13 mg, yield 17%).

¹H-NMR (CDCl₃, 400MHz): 2.00 (s, 3H), 3.47 (m, 2H), 3.84 (m, 2H), 4.08 (s, 6H), 6.36 (br, 1H), 6.89 (br, 1H), 7.32 - 7.40 (m, 5H), 7.55 (s, 1H), 7.86 (br, 1H), 8.61 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 442 (M⁺+1)

Example 520: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}-N'-(N-cyclohexylamino)thiourea

[0623] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 7 hr. Next, cyclohexylhydrazine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 12 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (8 mg, yield 10%).

¹H-NMR (CDCl₃, 400 MHz): 1.20 - 2.27 (m, 16H), 3.83 (m, 1H), 4.06 (s, 6H), 5.51 (m, 1H), 6.34 (m, 1H), 7.00 (m, 1H), 7.18 (m, 1H), 7.36 (m, 1H), 7.43 (s, 1H), 7.61 (s, 1H), 8.46 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 481 (M⁺+1)

Example 521: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}-N'-(1-piperidinyl)thiourea

[0624] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, 1-aminopiperidine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 14 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (20 mg, yield 27%).

¹H-NMR (CDCl₃, 400 MHz): 1.20 - 1.88 (m, 6H), 2.15 (s, 3H), 2.26 (s, 3H), 2.51 (m, 2H), 3.23 (m, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 6.33 (d, J = 5.4 Hz, 1H), 6.93 (br, 1H), 7.03 (d, J = 8.5 Hz, 1H), 7.47 (s, 1H), 7.57 (d, J = 8.6 Hz, 1H), 7.62 (s, 1H), 8.46 (d, J = 5.4 Hz, 1H), 9.00 (br, 1H)

Mass spectrometry value (ESI-MS, m/z): 467 (M⁺+1)

Example 522: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}-N'-(1-piperidinyl)thiourea

[0625] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 7 hr. Next, 1-aminopiperidine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 14 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (9 mg, yield 12%).

¹H-NMR (CDCl₃, 400 MHz): 1.20 - 1.90 (m, 6H), 2.18 (s, 3H), 2.27 (s, 3H), 2.50 (m, 2H), 3.21 (m, 2H), 4.07 (s, 6H), 6.38 (d, J = 5.4 Hz, 1H), 6.86 (br, 1H), 6.98 (s, 1H), 7.49 (s, 1H), 7.59 (s, 1H), 7.79 (s, 1H), 8.47 (d, J = 5.4 Hz, 1H), 9.05 (br, 1H)

Mass spectrometry value (ESI-MS, m/z): 467 (M⁺+1)

Example 523: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]-N'-(N-cyclohexylamino)thiourea

[0626] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (52 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 1.5 hr. Next, cyclohexylhydrazine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 7 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (10 mg, yield 13%).

¹H-NMR (CDCl₃, 400 MHz): 1.12 - 1.95 (m, 10H), 2.16 (s, 3H), 2.25 (s, 3H), 3.69 (m, 1H), 4.06 (s, 6H), 5.52 (m, 1H), 6.40 (d, J = 5.4 Hz, 1H), 6.97 (m, 1H), 7.46 (s, 1H), 7.52 (s, 1H), 7.59 (s, 1H), 8.47 (d, J = 5.4 Hz, 1H), 9.41 (br, 1H)

Mass spectrometry value (ESI-MS, m/z): 436 (?)

Example 524: N-[4-[(6,7-Dimethoxy-4-quinazolinyloxy)phenyl]-N'-(1-piperidinyl)thiourea

[0627] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (50 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (50 mg) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. Next, 1-aminopiperidine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 13 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (49 mg, yield 66%).

¹H-NMR (CDCl₃, 400 MHz): 1.18 - 1.83 (m, 6H), 2.48 (m, 2H), 3.18 (m, 2H), 4.07 (s, 3H), 4.08 (s, 3H), 6.99 (s, 1H), 7.26 (d, J = 8.1 Hz, 2H), 7.34 (s, 1H), 7.56 (s, 1H), 7.76 (d, J = 8.5 Hz, 2H), 7.53 (s, 1H), 8.61 (s, 1H), 9.27 (br, 1H)

Mass spectrometry value (ESI-MS, m/z): 440 (M⁺+1)

Example 525: N-[4-[(6,7-Dimethoxy-4-quinazolinyloxy)phenyl]-N'-[3-(2-oxotetrahydro-1H-1-pyrrolyl)propyl]thiourea

[0628] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (56 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (50 mg) was then added to the solution, and the mixture was stirred at room temperature for 7 hr. Next, 1-(3-aminopropyl)pyrrolidone (50 mg) was added thereto, and the mixture was further stirred at room temperature for 13 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (15 mg, yield 17%).

¹H-NMR (CDCl₃, 400 MHz): 1.87 (m, 2H), 2.04 (m, 2H), 2.37 (t, J = 8.2 Hz, 2H), 3.30 (t, J = 6.2 Hz, 2H), 3.41 (t, J = 7.2 Hz, 2H), 3.64 (m, 2H), 4.07 (s, 6H), 7.31 - 7.42 (m, 6H), 7.55 (s, 1H), 7.79 (br, 1H), 8.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 482 (M⁺+1)

Example 526: N-[4-[(6,7-Dimethoxy-4-quinazolinyloxy)phenyl]-N'-[3-(1-imidazolyl)propyl]thiourea

[0629] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (56 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (50 mg) was then added to the solution, and the mixture was stirred at room temperature for 7 hr. Next, 3-(1-imidazolyl)propylamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 13 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (16 mg, yield 18%).

¹H-NMR (CDCl₃, 400 MHz): 2.29 (m, 2H), 3.69 (m, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 4.38 (m, 2H), 7.20 - 7.57 (m, 11H), 8.58 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 465 (M⁺+1)

Example 527: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[2-(1-morpholinyl)ethyl]thiourea

[0630] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (56 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (50 mg) was then added to the solution, and the mixture was stirred at room temperature for 7 hr. Next, 2-(1-morpholinyl)ethylamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 13 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (9 mg, yield 10%).

¹H-NMR (CDCl₃, 400 MHz): 2.50 (m, 4H), 2.64 (m, 2H), 3.65 (m, 4H), 3.75 (m, 2H), 4.08 (s, 3H), 4.08 (s, 3H), 7.14 (br, 1H), 7.34 (m, 4H), 7.35 (s, 1H), 7.54 (s, 1H), 7.73 (br, 1H), 8.61 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 470 (M⁺+1)

Example 528: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[2-[N-ethyl-N-(o-tolyl)aminoethyl]thiourea

[0631] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (56 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (50 mg) was then added to the solution, and the mixture was stirred at room temperature for 7 hr. Next, N-ethyl-N-(o-tolyl)ethylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 13 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (22 mg, yield 22%).

¹H-NMR (CDCl₃, 400 MHz): 1.11 (t, J = 7.1 Hz, 3H), 2.29 (s, 2H), 3.34 (q, J = 7.1 Hz, 2H), 3.55 (t, J = 6.3 Hz, 2H), 3.84 (m, 2H), 4.08 (s, 6H), 6.43 (br, 1H), 6.54 - 6.61 (m, 3H), 7.10 (m, 1H), 7.19 (d, J = 8.8 Hz, 2H), 7.24 (d, J = 8.8 Hz, 2H), 7.35 (s, 1H), 7.53 (s, 1H), 7.77 (br, 1H), 8.60 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 518 (M⁺+1)

Example 529: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(2-dimethylaminoethyl)thiourea

[0632] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (50 mg) was then added to the solution, and the mixture was stirred at room temperature for 5 hr. Next, N,N-dimethylethylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 16 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (18 mg, yield 24%).

¹H-NMR (CDCl₃, 400 MHz): 1.83 (br, 2H), 2.26 (br, 6H), 2.55 (br, 2H), 4.07 (s, 6H), 7.29 - 7.30 (m, 5H), 7.34 (s, 1H), 7.54 (s, 1H), 8.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 428 (M⁺+1)

Example 530: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[2-(1-pyrrolidyl)ethyl]thiourea

[0633] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (50 mg) was then added to the solution, and the mixture was stirred at room temperature for 5 hr. Next, 2-(1-pyrrolidyl)ethylamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 16 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (16 mg, yield 21%).

¹H-NMR (CDCl₃, 400 MHz): 1.77 (br, 4H), 1.86 (br, 2H), 2.58 (br, 2H), 2.75 (br, 2H), 4.07 (s, 6H), 7.29 - 7.30 (m, 5H), 7.34 (s, 1H), 7.54 (s, 1H), 8.60 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 454 (M⁺+1)

Example 531: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(3-diethylaminopropyl)thiourea

[0634] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (50 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, N,N-diethylpropylenediamine (50 mg) was added thereto, and the mixture

was further stirred at room temperature for 15 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (10 mg, yield 12%).

¹H-NMR (CDCl₃, 400 MHz): 0.86 (br, 6H), 1.74 (br, 2H), 2.42 (br, 4H), 2.55 (br, 2H), 3.81 (br, 2H), 4.07 (s, 3H), 4.08 (s, 3H), 7.29 (s, 1H), 7.34 (m, 4H), 7.53 (s, 1H), 7.57 (br, 1H), 8.56 (s, 1H), 8.69 (br, 1H)

Mass spectrometry value (ESI-MS, m/z): 470 (M⁺+1)

Example 532: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(2-dibutylaminopropyl)thiourea

[0635] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (50 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, N,N-diethylpropylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 15 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (41 mg, yield 46%).

¹H-NMR (CDCl₃, 400 MHz): 0.87 (t, J = 7.1 Hz, 6H), 1.19 (m, 8H), 1.71 (m, 2H), 2.28 (m, 4H), 2.52 (m, 2H), 3.79 (m, 2H), 4.07 (s, 3H), 4.08 (s, 3H), 7.27 - 7.32 (m, 4H), 7.34 (s, 1H), 7.52 (s, 1H), 7.75 (br, 1H), 8.44 (br, 1H), 8.57 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 526 (M⁺+1)

Example 533: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[3-(1-morpholino)propyl]thiourea

[0636] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (50 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, 3-(1-morpholino)propylamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 15 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (16 mg, yield 20%).

¹H-NMR (CDCl₃, 400 MHz): 1.81 (m, 2H), 2.39 (m, 4H), 2.46 (m, 2H), 3.50 (m, 4H), 3.79 (m, 2H), 4.07 (s, 6H), 7.31 - 7.37 (m, 5H), 7.53 (s, 1H), 7.69 (br, 1H), 8.61 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 484 (M⁺+1)

Example 534: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[3-[1-(2-methylpiperidinyl)]propyl]thiourea

[0637] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (50 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, 3-[1-(2-methylpiperidinyl)]propylamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 15 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (30 mg, yield 36%).

¹H-NMR (CDCl₃, 400 MHz): 0.99 (d, J = 6.4 Hz, 3H), 1.24 - 2.53 (m, 11H), 2.81 (m, 2H), 3.71 (m, 1H), 3.81 (m, 1H), 4.07 (s, 3H), 4.07 (s, 3H), 7.29 - 7.37 (m, 5H), 7.52 (s, 1H), 7.74 (br, 1H), 7.83 (br, 1H), 8.59 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 496 (M⁺+1)

Example 535: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(2-diisopropylaminoethyl)thiourea

[0638] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (50 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, N,N-diisopropylethylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 15 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (47 mg, yield 58%).

¹H-NMR (CDCl₃, 400 MHz): 0.91 (br, 12H), 2.67 (br, 2H), 2.96 (br, 2H), 3.64 (br, 2H), 4.07 (s, 3H), 4.08 (s, 3H), 7.17 (br, 1H), 7.28 - 7.34 (m, 4H), 7.34 (s, 1H), 7.54 (s, 1H), 7.85 (br, 1H), 8.58 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 484 (M⁺+1)

Example 536: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[3-[1-(4-methylpiperazinyl)]propyl]thiourea

[0639] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (50 mg) was then added to the solution, and the mixture was stirred at room temperature for 1 hr. Next, 1-(3-aminopropyl)-4-methylpiperazine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 6 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (6 mg, yield 7%).

¹H-NMR (CDCl₃, 400 MHz): 1.75 - 1.83 (m, 6H), 2.23 (s, 3H), 2.23 (m, 2H), 2.44 (m, 4H), 3.78 (br, 2H), 4.06 (s, 3H), 4.08 (s, 3H), 7.31 - 7.34 (m, 5H), 7.51 (s, 1H), 7.59 (br, 1H), 8.61 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 497 (M⁺+1)

Example 537: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[3-(1-pyrrolidinyl)propyl]thiourea

[0640] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (50 mg) was then added to the solution, and the mixture was stirred at room temperature for 1 hr. Next, N,N-diethylpropylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 6 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (19 mg, yield 24%).

¹H-NMR (CDCl₃, 400 MHz): 1.55 (br, 2H), 1.79 (m, 2H), 2.42 (br, 4H), 2.58 (br, 2H), 3.81 (br, 2H), 4.07 (s, 3H), 4.07 (s, 3H), 7.27 - 7.34 (m, 4H), 7.34 (s, 1H), 7.52 (s, 1H), 7.73 (br, 1H), 8.19 (br, 1H), 8.59 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 467 (M⁺+1)

Example 538: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}-N'-(2-dimethylaminoethyl)thiourea

[0641] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, N,N-dimethylethylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 16 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (24 mg, yield 34%).

¹H-NMR (CDCl₃, 400 MHz): 2.16 (s, 3H), 2.22 (br, 6H), 2.28 (s, 3H), 2.51 (br, 2H), 3.68 (br, 2H), 4.06 (s, 3H), 4.06 (s, 3H), 6.27 (m, 1H), 6.68 (br, 1H), 7.05 (s, 1H), 7.21 (s, 1H), 7.44 (s, 1H), 7.49 (br, 1H), 7.57 (s, 1H), 8.46 (d, J = 5.2 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 455 (M⁺+1)

Example 539: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}-N'-[3-(1-imidazolyl)propyl]thiourea

[0642] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, 1-(3-aminopropyl)imidazole (50 mg) was added thereto, and the mixture was further stirred at room temperature for 16 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (20 mg, yield 25%).

¹H-NMR (CDCl₃, 400 MHz): 2.00 (m, 2H), 2.15 (m, 2H), 2.18 (s, 3H), 2.25 (s, 3H), 3.67 (m, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 5.98 (br, 1H), 6.33 (d, J = 5.4 Hz, 1H), 6.93 (s, 1H), 7.04 (s, 1H), 7.05 (s, 1H), 7.17 (s, 1H), 7.43 (s, 1H), 7.50 (br, 1H), 7.54 (s, 1H), 7.74 (s, 1H), 8.47 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

Example 540: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}-N'-[2-[N-ethyl-N-(o-tolyl)amino]ethyl]thiourea

[0643] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, N,N-dimethylethylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 16 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (28 mg, yield 32%).

¹H-NMR (CDCl₃, 400 MHz): 1.07 (t, J = 7.1 Hz, 3H), 2.07 (s, 3H), 2.22 (s, 3H), 2.29 (s, 3H), 3.30 (q, J = 7.1 Hz, 2H), 3.51 (t, J = 6.0 Hz, 2H), 3.84 (m, 2H), 4.06 (s, 3H), 4.06 (s, 3H), 6.06 (br, 1H), 6.22 (d, J = 5.4 Hz, 1H), 6.53 - 6.68 (m, 3H), 6.99 (s, 1H), 7.02 (s, 1H), 7.09 (m, 1H), 7.45 (s, 1H), 7.52 (br, 1H), 7.54 (s, 1H), 8.43 (d, J = 5.2 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 545 (M⁺+1)

Example 541: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}-N'-[2-(1-pyrrolidinyl)ethyl]thiourea

[0644] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, 1-(2-aminoethyl)pyrrolidine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 16 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (8 mg, yield 10%).

¹H-NMR (CDCl₃, 400 MHz): 1.72 (br, 4H), 2.16 (s, 3H), 2.27 (s, 3H), 2.54 (br, 4H), 2.73 (br, 2H), 3.72 (br, 2H), 4.06 (s, 6H), 6.28 (m, 1H), 6.77 (br, 1H), 7.04 (s, 1H), 7.19 (s, 1H), 7.43 (s, 1H), 7.56 (s, 1H), 8.46 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 481 (M⁺+1)

Example 542: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}-N'-(2-dimethylaminoethyl)thiourea

[0645] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 7 hr. Next, N,N-dimethylethylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 13 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (12 mg, yield 17%).

¹H-NMR (CDCl₃, 400 MHz): 2.16 (s, 3H), 2.19 (br, 6H), 2.28 (s, 3H), 2.48 (br, 2H), 3.66 (br, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 6.22 (m, 1H), 6.56 (br, 1H), 7.04 (d, J = 8.3 Hz, 1H), 7.19 (d, J = 8.5 Hz, 1H), 7.44 (s, 1H), 7.60 (s, 1H), 8.45 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 455 (M⁺+1)

Example 543: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}-N'-[3-(1-imidazolyl)propyl]thiourea

[0646] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 7 hr. Next, 1-(3-aminopropyl)imidazole (50 mg) was added thereto, and the mixture was further stirred at room temperature for 13 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (13 mg, yield 17%).

¹H-NMR (CDCl₃, 400MHz): 2.14 (m, 2H), 2.18 (s, 3H), 2.26 (s, 3H), 3.66 (m, 2H), 4.04 (m, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 5.79 (br, 1H), 6.30 (d, J = 5.4 Hz, 1H), 6.92 (s, 1H), 7.04 (s, 1H), 7.05 (d, J = 8.6 Hz, 1H), 7.14 (d, J = 8.6 Hz, 1H), 7.44 (s, 1H), 7.51 (br, 1H), 7.56 (s, 1H), 7.62 (s, 1H), 8.47 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

Example 544: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}-N'-[2-[N-ethyl-N-(o-tolyl)amino]ethyl]thiourea

[0647] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 7 hr. Next, N,N-dimethylethylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 13 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (4 mg, yield 4%).

¹H-NMR (CDCl₃, 400 MHz): 1.06 (t, J = 7.1 Hz, 3H), 2.10 (s, 3H), 2.21 (s, 3H), 2.28 (s, 3H), 3.28 (q, J = 7.1 Hz, 2H), 3.49 (t, J = 6.1 Hz, 2H), 3.83 (m, 2H), 4.07 (s, 6H), 5.94 (br, 1H), 6.18 (d, J = 5.1 Hz, 1H), 6.49 - 7.10 (m, 6H), 7.46 (s, 1H), 7.50 (br, 1H), 7.57 (s, 1H), 8.42 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 545 (M⁺+1)

Example 545: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}-N'-[2-(1-morpholino)ethyl]thiourea

[0648] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, 1-(2-aminoethyl)morpholine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 16 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (23 mg, yield 29%).

¹H-NMR (CDCl₃, 400 MHz): 2.19 (s, 3H), 2.28 (s, 3H), 2.43 (br, 4H), 2.58 (m, 2H), 3.56 (m, 4H), 3.71 (m, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 6.30 (d, J = 5.1 Hz, 1H), 6.60 (br, 1H), 7.07 (s, 1H), 7.21 (s, 1H), 7.45 (s, 1H), 7.46 (br, 1H), 7.56 (s, 1H), 8.48 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 497 (M⁺+1)

Example 546: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}-N'-(3-diethylaminopropyl)thiourea

[0649] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, N,N-diethylpropylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 15 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (36 mg, yield 45%).

¹H-NMR (CDCl₃, 400 MHz): 0.83 (t, J = 7.1 Hz, 6H), 1.70 (m, 2H), 2.16 (s, 3H), 2.29 (s, 3H), 2.32 (m, 4H), 2.49 (m, 2H), 3.78 (m, 2H), 4.06 (s, 3H), 4.06 (s, 3H), 6.30 (d, J = 5.4 Hz, 1H), 7.00 (d, J = 8.5 Hz, 1H), 7.19 (d, J = 8.5 Hz, 1H), 7.44 (s, 1H), 7.56 (br, 1H), 7.57 (s, 1H), 7.80 (br, 1H), 8.46 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 497 (M⁺+1)

Example 547: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}-N'-(3-dibutylaminopropyl)thiourea

[0650] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, N,N-dibutylpropylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 15 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (33 mg, yield 37%).

¹H-NMR (CDCl₃, 400 MHz): 0.89 (t, J = 6.8 Hz, 6H), 1.19 (m, 8H), 1.69 (m, 2H), 2.15 (s, 3H), 2.29 (s, 3H), 2.49 (m, 2H), 3.78 (m, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 6.30 (d, J = 5.1 Hz, 1H), 7.01 (d, J = 8.6 Hz, 1H), 7.19 (d, J = 8.5 Hz, 1H), 7.44 (s, 1H), 7.48 (br, 1H), 7.56 (s, 1H), 7.79 (br, 1H), 8.46 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 552 (M⁺+1)

Example 548: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}-N'-[3-(1-morpholino)propyl]thiourea

[0651] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, 1-(3-aminopropyl)morpholine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 15 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (16 mg, yield 19%).

¹H-NMR (CDCl₃, 400 MHz): 1.78 (m, 4H), 2.19 (s, 3H), 2.29 (s, 3H), 2.36 (m, 4H), 3.45 (m, 4H), 3.78 (m, 2H), 4.06 (s, 3H), 4.06 (s, 3H), 6.33 (d, J = 5.1 Hz, 1H), 6.70 (br, 1H), 7.03 (d, J = 8.6 Hz, 1H), 7.19 (d, J = 8.5 Hz, 1H), 7.44 (s, 1H), 7.56 (s, 1H), 8.48 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 511 (M⁺+1)

Example 549: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}-N'-[3-(2-methylpiperidinyl)propyl]thiourea

[0652] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, 1-(3-aminopropyl)-2-methylpiperidine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 15 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (39 mg, yield 47%).

¹H-NMR (CDCl₃, 400 MHz): 0.94 - 2.20 (m, 14H), 2.17 (s, 3H), 2.29 (s, 3H), 2.76 (m, 2H), 3.68 (m, 1H), 3.85 (m, 1H), 4.05 (s, 3H), 4.06 (s, 3H), 6.34 (d, J = 5.1 Hz, 1H), 7.02 (d, J = 8.6 Hz, 1H), 7.20 (d, J = 8.3 Hz, 1H), 7.44 (s, 1H), 7.50 (br, 1H), 7.55 (s, 1H), 8.48 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 523 (M⁺)

Example 550: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}-N'-(2-diisopropylaminoethyl)thiourea

[0653] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, N,N-diisopropylethylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 15 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (52 mg, yield 64%).

¹H-NMR (CDCl₃, 400 MHz): 0.84 (br, 12H), 2.13 (s, 3H), 2.27 (s, 3H), 2.62 (m, 2H), 2.89 (m, 2H), 3.61 (m, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 6.24 (m, 1H), 7.02 (d, J = 8.5 Hz, 1H), 7.18 (d, J = 8.3 Hz, 1H), 7.44 (s, 1H), 7.52 (br, 1H), 7.58 (s, 1H), 8.44 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 511 (M⁺+1)

Example 551: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}-N'-(3-diethylaminopropyl)thiourea

[0654] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, N,N-diethylpropylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 16 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (38 mg, yield 49%).

¹H-NMR (CDCl₃, 400 MHz): 0.86 (t, J = 7.2 Hz, 6H), 1.72 (m, 2H), 2.16 (s, 3H), 2.27 (s, 3H), 2.34 (m, 4H), 2.51 (m, 2H), 3.79 (m, 2H), 4.06 (s, 6H), 6.34 (d, J = 5.1 Hz, 1H), 7.01 (s, 1H), 7.21 (s, 1H), 7.38 (br, 1H), 7.44 (s, 1H), 7.54 (s, 1H), 7.93 (br, 1H), 8.48 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 497 (M⁺+1)

Example 552: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}-N'-(3-dibutylaminopropyl)thiourea

[0655] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, N,N-dibutylpropylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 16 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (34 mg, yield 40%).

¹H-NMR (CDCl₃, 400 MHz): 0.90 (t, J = 7.0 Hz, 6H), 1.20 (m, 8H), 1.70 (m, 2H), 2.16 (s, 3H), 2.23 (m, 4H), 2.27 (s, 3H), 2.51 (m, 2H), 3.79 (m, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 6.34 (d, J = 5.2 Hz, 1H), 7.02 (s, 1H), 7.20 (s, 1H), 7.30 (br, 1H), 7.44 (s, 1H), 7.54 (s, 1H), 7.88 (br, 1H), 8.48 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 553 (M⁺+1)

Example 553: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}-N'-[3-(1-morpholino)propyl]thiourea

[0656] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, 1-(3-aminopropyl)morpholine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 16 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (18 mg, yield 23%).

¹H-NMR (CDCl₃, 400 MHz): 1.78 (m, 4H), 2.19 (s, 3H), 2.27 (s, 3H), 2.36 (m, 4H), 3.45 (m, 4H), 3.79 (m, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 6.37 (d, J = 5.4 Hz, 1H), 6.83 (br, 1H), 7.03 (s, 1H), 7.22 (s, 1H), 7.44 (s, 1H), 7.54 (s, 1H), 8.50 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 511 (M⁺+1)

Example 554: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}-N'-[3-(2-methylpiperidinyl)propyl]thiourea

[0657] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, 1-(3-aminopropyl)-2-methylpiperidine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 16 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (46 mg, yield 56%).

¹H-NMR (CDCl₃, 400 MHz): 0.90 - 2.20 (m, 14H), 2.17 (s, 3H), 2.27 (s, 3H), 2.79 (m, 2H), 3.68 (m, 1H), 3.88 (m, 1H), 4.04 (s, 3H), 4.06 (s, 3H), 6.39 (d, J = 5.2 Hz, 1H), 7.02 (s, 1H), 7.22 (s, 1H), 7.38 (br, 1H), 7.44 (s, 1H), 7.53 (s, 1H), 8.49 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 523 (M⁺)

Example 555: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}-N'-(2-diisopropylaminoethyl)thiourea

[0658] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, N,N-diisopropylethylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 16 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (13 mg, yield 17%).

¹H-NMR (CDCl₃, 400 MHz): 0.86 (br, 12H), 2.14 (s, 3H), 2.26 (s, 3H), 2.62 (m, 2H), 2.91 (m, 2H), 3.61 (m, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 6.27 (m, 1H), 6.68 (br, 1H), 7.03 (s, 1H), 7.19 (s, 1H), 7.36 (br, 1H), 7.44 (s, 1H), 7.56 (s, 1H), 8.46 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 511 (M⁺+1)

Example 556: N-{4-[(6,7-Dimethoxy-4-quinolyloxy)-2,5-dimethylphenyl]-N'-[3-(4-methylpiperazinyl)propyl]}thiourea

[0659] 4-[(6,7-Dimethoxy-4-quinolyloxy)-2,5-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, 1-(3-aminopropyl)-4-methylpiperazine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 16 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (20 mg, yield 24%).

¹H-NMR (CDCl₃, 400 MHz): 1.76 (m, 6H), 2.17 (s, 3H), 2.26 (m, 2H), 2.28 (s, 3H), 2.41 (m, 4H), 3.77 (m, 2H), 4.03 (s, 3H), 4.06 (s, 3H), 6.34 (d, J = 5.1 Hz, 1H), 6.83 (br, 1H), 7.05 (s, 1H), 7.22 (s, 1H), 7.37 (br, 1H), 7.44 (s, 1H), 7.52 (s, 1H), 8.48 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 524 (M⁺+1)

Example 557: N-{4-[(6,7-Dimethoxy-4-quinolyloxy)-2,3-dimethylphenyl]-N'-[3-(4-methylpiperazinyl)propyl]}thiourea

[0660] 4-[(6,7-Dimethoxy-4-quinolyloxy)-2,3-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, 1-(3-aminopropyl)-4-methylpiperazine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 16 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (10 mg, yield 11%).

¹H-NMR (CDCl₃, 400 MHz): 1.73 (m, 6H), 2.17 (s, 3H), 2.25 (m, 2H), 2.29 (s, 3H), 2.39 (m, 4H), 3.77 (m, 2H), 4.04 (s, 3H), 4.06 (s, 3H), 6.30 (d, J = 5.1 Hz, 1H), 6.76 (br, 1H), 7.05 (d, J = 8.6 Hz, 1H), 7.20 (d, J = 8.6 Hz, 1H), 7.38 (br, 1H), 7.44 (s, 1H), 7.55 (s, 1H), 8.47 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 524 (M⁺+1)

Example 558: N-{4-[(6,7-Dimethoxy-4-quinolyloxy)-2,3-dimethylphenyl]-N'-[3-(1-piperidinyl)propyl]}thiourea

[0661] 4-[(6,7-Dimethoxy-4-quinolyloxy)-2,3-dimethylaniline (51 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, 1-(3-aminopropyl)pyrrolidine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 16 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (18 mg, yield 22%).

¹H-NMR (CDCl₃, 400 MHz): 1.55 (br, 4H), 1.77 (br, 2H), 2.17 (s, 3H), 2.28 (s, 3H), 2.39 (br, 4H), 2.55 (br, 2H), 3.78 (br, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 6.32 (d, J = 5.4 Hz, 1H), 7.00 (d, J = 8.6 Hz, 1H), 7.18 (m, 1H), 7.44 (s, 1H), 7.46 (br, 1H), 7.56 (s, 1H), 8.47 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 475

Example 559: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(2-dimethylaminoethyl)thiourea

[0662] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 5 hr. Next, N,N-dimethylethylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 15 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (62 mg, yield 83%).

¹H-NMR (CDCl₃, 400 MHz): 2.52 (s, 6H), 2.67 (br, 2H), 3.68 (br, 2H), 4.07 (s, 6H), 7.26 - 7.54 (m, 7H), 7.83 (br, 1H), 8.59 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 428 (M⁺+1)

Example 560: N-(1-Benzyltetrahydro-1H-3-pyrrolyl)-N'-{4-[(6,7-dimethoxy-4-quinolyloxy)phenyl]}urea

[0663] Chloroform (10 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinolyloxy)aniline (100 mg)

to prepare a solution. Triphosgene (110 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. 1-Benzyl-3-aminopyrrolidine (89 mg) was then added thereto, and the mixture was stirred at room temperature for 3 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (76 mg, yield 45%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.97 - 2.08 (m, 1H), 2.38 - 2.49 (m, 1H), 2.55 - 2.64 (m, 1H), 2.78 - 2.85 (m, 1H), 3.13 - 3.19 (m, 1H), 3.34 - 3.41 (m, 1H), 3.91 (s, 1H), 3.92 (s, 1H), 4.04 (s, 6H), 4.45 - 4.53 (m, 1H), 6.23 (br, 1H), 6.44 (d, J = 5.4 Hz, 1H), 7.07 - 7.11 (m, 2H), 7.35 - 7.47 (m, 8H), 7.56 (s, 1H), 8.46 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 499 (M⁺+1)

Example 561: Ethyl 4-[(4-[(6,7-dimethoxy-4-quinolyl)oxy]anilino)carbonyl]amino]-1-piperidine-carboxylate

[0664] Chloroform (10 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (100 mg) to prepare a solution. Triphosgene (110 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. Ethyl 4-amino-1-piperidine (87 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (108 mg, yield 65%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.25 (t, J = 7.1 Hz, 3H), 1.32 - 1.45 (m, 2H), 1.93 - 2.02 (m, 2H), 2.92 - 3.05 (m, 2H), 3.83 - 3.94 (m, 1H), 3.98 - 4.06 (m, 2H), 4.07 (s, 3H), 4.08 (s, 3H), 4.09 - 4.16 (m, 2H), 5.57 (d, J = 7.8 Hz, 1H), 6.48 (d, J = 5.9 Hz, 1H), 7.05 - 7.10 (m, 2H), 7.50 - 7.55 (m, 2H), 7.58 (s, 1H), 7.59 (s, 1H), 7.74 (s, 1H), 8.36 (d, J = 5.9 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 495 (M⁺+1)

Example 562: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2,2,6,6-tetramethyl-4-piperidyl)urea

[0665] Chloroform (10 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (100 mg) to prepare a solution. Triphosgene (110 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. 4-Amino-2,2,6,6-tetramethylpiperidine (79 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution; and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (27 mg, yield 17%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.53 - 2.09 (m, 16H), 4.02 (s, 3H), 4.06 (s, 3H), 4.22 - 4.37 (m, 1H), 6.51 (d, J = 5.6 Hz, 1H), 7.05 (d, J = 8.8 Hz, 2H), 7.42 (s, 1H), 7.54 - 7.64 (m, 3H), 8.42 (d, J = 5.9 Hz, 1H), 8.65 (br, 1H)

Mass spectrometry value (ESI-MS, m/z): 479 (M⁺+1)

Example 563: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(2,2,6,6-tetramethyl-4-piperidyl)urea

[0666] Chloroform (10 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (100 mg) to prepare a solution. Triphosgene (110 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. 4-Amino-2,2,6,6-tetramethylpiperidine (79 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (66 mg, yield 41%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.28 - 2.09 (m, 16H), 4.05 (s, 3H), 4.06 (s, 3H), 4.11 - 4.28 (m, 1H), 7.13 (d, J = 8.8 Hz, 2H), 7.29 (s, 1H), 7.46 - 7.55 (m, 3H), 8.57 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 480 (M⁺+1)

Example 564: N-[(3R)-1-Benzyltetrahydro-1H-3-pyrrolyl]-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]urea

[0667] Chloroform (10 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (100 mg) to prepare a solution. Triphosgene (110 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. (3R)-(-)-1-Benzyl-3-aminopyrrolidine (89 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (54 mg, yield 32%).

¹H-NMR (chloroform-d, 400 MHz): δ 2.00 - 2.16 (m, 2H), 2.41 - 2.52 (m, 1H), 2.63 - 2.72 (m, 1H), 2.84 - 2.92 (m, 1H), 3.21 - 3.29 (m, 1H), 3.99 (s, 1H), 4.01 (s, 1H), 4.04 (s, 3H), 4.05 (s, 3H), 4.50 - 4.61 (m, 1H), 6.44 (d, J = 5.1 Hz, 1H), 7.06 - 7.12 (m, 2H), 7.37 - 7.48 (m, 8H), 7.56 (s, 1H), 8.46 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 499 (M⁺+1)

Example 565: N-[(3S)-1-Benzyltetrahydro-1H-3-pyrrolyl]-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]urea

[0668] Chloroform (10 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (100 mg) to prepare a solution. Triphosgene (110 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. (3S)-(+)-1-Benzyl-3-aminopyrrolidine (89 mg) was then added thereto, and the mixture was stirred at room temperature for 5 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (48 mg, yield 29%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.92 - 2.17 (m, 2H), 2.40 - 2.51 (m, 1H), 2.60 - 2.71 (m, 1H), 2.81 - 2.90 (m, 1H), 3.18 - 3.25 (m, 1H), 3.96 (s, 1H), 3.98 (s, 1H), 4.05 (s, 6H), 4.49 - 4.58 (m, 1H), 6.44 (d, J = 5.1 Hz, 1H), 7.06 - 7.12 (m, 2H), 7.37 - 7.49 (m, 7H), 7.56 (s, 1H), 7.61 (s, 1H), 8.46 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 499 (M⁺+1)

Example 566: N-[(3R)-1-Benzyltetrahydro-1H-3-pyrrolyl]-N'-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]urea

[0669] Chloroform (10 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (100 mg) to prepare a solution. Triphosgene (110 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. (3R)-(-)-1-Benzyl-3-aminopyrrolidine (89 mg) was then added thereto, and the mixture was stirred at room temperature for 5 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (114 mg, yield 68%).

¹H-NMR (chloroform-d, 400 MHz): δ 2.07 - 2.20 (m, 1H), 2.40 - 2.52 (m, 1H), 2.76 - 2.87 (m, 1H), 2.99 - 3.07 (m, 1H), 3.29 - 3.38 (m, 1H), 3.51 - 3.60 (m, 1H), 4.06 (s, 6H), 4.08 (s, 1H), 4.10 (s, 1H), 4.57 - 4.66 (m, 1H), 6.75 - 6.85 (m, 1H), 7.11 - 7.17 (m, 2H), 7.29 - 7.57 (m, 9H), 8.59 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 500 (M⁺+1)

Example 567: N-[(3S)-1-Benzyltetrahydro-1H-3-pyrrolyl]-N'-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]urea

[0670] Chloroform (10 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (100 mg) to prepare a solution. Triphosgene (110 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. (3S)-(+)-1-Benzyl-3-aminopyrrolidine (89 mg) was then added thereto, and the mixture was stirred at room temperature for 5 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound

(100 mg, yield 60%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.97 - 2.08 (m, 1H), 2.33 - 2.48 (m, 1H), 2.60 - 2.69 (m, 1H), 2.82 - 2.91 (m, 1H), 3.11 - 3.20 (m, 1H), 3.32 - 3.42 (m, 1H), 3.94 (s, 1H), 3.96 (s, 1H), 4.06 (s, 6H), 4.46 - 4.57 (m, 1H), 6.37 (br, 1H), 7.12 - 7.18 (m, 2H), 7.29 - 7.50 (m, 8H), 7.54 (s, 1H), 8.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 500 (M⁺+1)

Example 568: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-[1-(2-methylbenzyl)-4-piperidyl]urea

[0671] N-(1-Benzyl-4-piperidyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]urea (100 mg) was dissolved in 1,2-dichloroethane (25 ml) to prepare a solution. 1-Chloroethyl chloroformate (0.10 ml) was then added to the solution, and the mixture was heated under reflux overnight. The solvent was removed by distillation under the reduced pressure. Methanol (20 ml) was added to the residue, followed by heating under reflux for 2 hr. The solvent was removed by distillation under the reduced pressure to give 139 mg of N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(4-piperidyl) urea (1).

[0672] Acetonitrile (10 ml) was added to the compound (1) (139 mg), 2-methylbenzyl bromide (0.03 ml), and potassium carbonate (81 mg), and the mixture was stirred at room temperature overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (46 mg, yield 45%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.88 - 2.01 (m, 2H), 2.09 - 2.19 (m, 2H), 2.42 (s, 3H), 2.53 - 2.67 (m, 2H), 3.19 - 3.29 (m, 2H), 3.30 - 3.39 (m, 1H), 3.90 (s, 2H), 4.04 (s, 3H), 4.04 (s, 3H), 6.42 (d, J = 5.4 Hz, 1H), 7.05 - 7.12 (m, 2H), 7.17 - 7.27 (m, 4H), 7.42 (s, 1H), 7.47 - 7.53 (m, 2H), 7.55 (s, 1H), 7.56 (s, 1H), 8.45 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 527 (M⁺+1)

Example 569: N-[4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl]-N'-[1-(2-methylbenzyl)tetrahydro-1H-3-pyrrolyl]urea

[0673] 3-Aminopyrrolidine (500 mg) was dissolved in acetonitrile (10 ml) to prepare a solution. 2-Methylbenzyl bromide (0.78 ml) and potassium carbonate (2.40 g) were added to the solution, and the mixture was stirred at room temperature for 3 hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform/methanol for development to give 1-(2-methylbenzyl)-3-pyrrolidinamine (1) (604 mg, yield 55%).

[0674] Chloroform (10 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (100 mg) to prepare a solution. Triphosgene (110 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. The compound (1) (96 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (64 mg, yield 37%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.95 - 2.05 (m, 1H), 2.41 (s, 3H), 2.40 - 2.48 (m, 1H), 2.55 - 2.63 (m, 1H), 2.79 - 2.87 (m, 1H), 3.08 - 3.14 (m, 1H), 3.30 - 3.38 (m, 1H), 3.90 (s, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 4.44 - 4.55 (m, 1H), 7.13 - 7.18 (m, 2H), 7.18 - 7.40 (m, 5H), 7.40 - 7.47 (m, 2H), 7.55 (s, 1H), 8.60 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 514 (M⁺+1)

Example 570: N-[4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl]-N'-[1-(2-methylbenzyl)tetrahydro-1H-3-pyrrolyl]urea

[0675] Chloroform (13 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitro-aniline (100 mg) to prepare a solution. Triphosgene (96 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. 1-(2-Methylbenzyl)-3-pyrrolidinamine (83 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the

title compound (38 mg, yield 23%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.94 - 2.04 (m, 1H), 2.44 (s, 3H), 2.42 - 2.50 (m, 1H), 2.55 - 2.65 (m, 1H), 2.81 - 2.90 (m, 1H), 3.02 - 3.10 (m, 1H), 3.27 - 3.34 (m, 1H), 3.88 - 3.92 (m, 2H), 4.07 (s, 3H), 4.09 (s, 3H), 4.50 - 4.59 (m, 1H), 7.18 - 7.26 (m, 2H), 7.32 - 7.43 (m, 2H), 7.49 - 7.55 (m, 2H), 8.12 (d, J = 2.7 Hz, 1H), 8.60 (s, 1H), 8.71 - 8.77 (m, 1H), 9.78 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 559 (M⁺+1)

Example 571: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-methoxyphenyl}-N'-[1-(2-methylbenzyl)tetrahydro-1H-3-pyrrolyl]urea

[0676] Chloroform (10 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-methoxyaniline (100 mg) to prepare a solution. Triphosgene (99 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. 1-(2-Methylbenzyl)-3-pyrrolidinamine (87 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (58 mg, yield 35%).

¹H-NMR (chloroform-d, 400 MHz): δ 2.01 - 2.11 (m, 1H), 2.21 - 2.33 (m, 1H), 2.50 (s, 3H), 2.48 - 2.58 (m, 1H), 2.86 - 2.98 (m, 1H), 3.43 - 3.52 (m, 1H), 3.68 - 3.78 (m, 1H), 3.84 (s, 3H), 4.07 (s, 6H), 4.21 (s, 1H), 4.23 (s, 1H), 4.71 - 4.82 (m, 1H), 6.75 (d, J = 2.4 Hz, 1H), 6.79 (dd, J = 2.4 Hz, 8.8 Hz, 1H), 7.17 - 7.22 (m, 1H), 7.27 - 7.36 (m, 3H), 7.54 (s, 1H), 7.54 - 7.59 (m, 1H), 8.13 (d, J = 8.8 Hz, 1H), 8.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 544 (M⁺+1)

Example 572: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}-N'-[1-(2-methylbenzyl)tetrahydro-1H-3-pyrrolyl]urea

[0677] Chloroform (10 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (100 mg) to prepare a solution. Triphosgene (101 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. 1-(2-Methylbenzyl)-3-pyrrolidinamine (88 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (68 mg, yield 41%).

¹H-NMR (chloroform-d, 400 MHz): δ 2.01 - 2.10 (m, 1H), 2.11 (s, 3H), 2.22 (s, 3H), 2.36 (s, 3H), 2.38 - 2.47 (m, 1H), 2.50 - 2.59 (m, 1H), 2.73 - 2.81 (m, 1H), 3.01 - 3.09 (m, 1H), 3.23 - 3.33 (m, 1H), 3.86 (s, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 4.48 - 4.58 (m, 1H), 6.30 (d, J = 5.4 Hz, 1H), 6.97 (d, J = 8.8 Hz, 1H), 7.14 - 7.36 (m, 4H), 7.44 (s, 1H), 7.62 (s, 1H), 8.44 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 541 (M⁺+1)

Example 573: N-[2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]-N'-[1-(2-methylbenzyl)tetrahydro-1H-3-pyrrolyl]urea

[0678] Chloroform (10 ml) and triethylamine (2 ml) were added to 2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (100 mg) to prepare a solution. Triphosgene (99 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. 1-(2-Methylbenzyl)-3-pyrrolidinamine (86 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (82 mg, yield 50%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.92 - 2.01 (m, 1H), 2.39 - 2.47 (m, 1H), 2.41 (s, 3H), 2.51 - 2.60 (m, 1H), 2.77 - 2.84 (m, 1H), 3.01 - 3.08 (m, 1H), 3.23 - 3.33 (m, 1H), 3.86 (s, 1H), 3.87 (s, 1H), 4.07 (s, 6H), 4.27 - 4.38 (m, 1H), 7.12 - 7.40 (m, 7H), 7.51 (s, 1H), 8.19 (d, J = 9.0 Hz, 1H), 8.61 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 548 (M⁺+1)

Example 574: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-[1-(2-methylbenzyl)tetrahydro-1H-3-pyrrolyl]urea

[0679] Chloroform (10 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (100 mg) to prepare a solution. Triphosgene (110 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. 1-(2-Methylbenzyl)-3-pyrrolidinamine (96 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (101 mg, yield 59%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.98 - 2.10 (m, 1H), 2.38 - 2.50 (m, 1H), 2.41 (s, 3H), 2.58 - 2.68 (m, 1H), 2.83 - 2.93 (m, 1H), 3.15 - 3.22 (m, 1H), 3.37 - 3.44 (m, 1H), 3.95 (s, 2H), 4.04 (s, 6H), 4.46 - 4.58 (m, 1H), 6.43 (d, J = 5.4 Hz, 1H), 7.05 - 7.12 (m, 2H), 7.18 - 7.47 (m, 7H), 7.56 (s, 1H), 8.46 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 513 (M⁺+1)

Example 575: N-[(3R)-1-Benzyltetrahydro-1H-3-pyrrolyl]-N'-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl]urea

[0680] Chloroform (15 ml) and triethylamine (3 ml) were added to 2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy]aniline (200 mg) to prepare a solution. Triphosgene (198 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. (3R)-(-)-1-Benzyl-3-aminopyrrolidine (80 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (189 mg, yield 59%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.90 - 2.02 (m, 1H), 2.37 - 2.47 (m, 1H), 2.48 - 2.58 (m, 1H), 2.72 - 2.80 (m, 1H), 2.98 - 3.06 (m, 1H), 3.21 - 3.29 (m, 1H), 3.83 (s, 1H), 3.85 (s, 1H), 4.07 (s, 6H), 4.45 - 4.56 (m, 1H), 7.14 (dd, J = 2.7 Hz, 9.0 Hz, 1H), 7.28 - 7.43 (m, 7H), 7.51 (s, 1H), 8.20 (d, J = 9.0 Hz, 1H), 8.61 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 534 (M⁺+1)

Example 576: N-[(3S)-1-Benzyltetrahydro-1H-3-pyrrolyl]-N'-[2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl]urea

[0681] Chloroform (15 ml) and triethylamine (3 ml) were added to 2-chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy]aniline (200 mg) to prepare a solution. Triphosgene (198 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. (3S)-(+)-1-Benzyl-3-aminopyrrolidine (80 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (204 mg, yield 63%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.90 - 2.00 (m, 1H), 2.35 - 2.48 (m, 1H), 2.50 - 2.58 (m, 1H), 2.73 - 2.80 (m, 1H), 2.98 - 3.05 (m, 1H), 3.20 - 3.29 (m, 1H), 3.83 (s, 1H), 3.85 (s, 1H), 4.07 (s, 6H), 4.45 - 4.54 (m, 1H), 7.15 (dd, J = 2.7 Hz, 9.0 Hz, 1H), 7.28 - 7.43 (m, 7H), 7.51 (s, 1H), 8.20 (d, J = 9.0 Hz, 1H), 8.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 534 (M⁺+1)

Example 577: N-[(3R)-1-Benzyltetrahydro-1H-3-pyrrolyl]-N'-{4-[(6,7-dimethoxy-4-quinazolinyloxy)-2-nitrophenyl]urea

[0682] Chloroform (27 ml) and triethylamine (4 ml) were added to 4-[(6,7-dimethoxy-4-quinazolinyloxy)-2-nitroaniline (200 mg) to prepare a solution. Triphosgene (192 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. (3R)-(-)-1-Benzyl-3-aminopyrrolidine (77 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the

reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (184 mg, yield 58%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.96 - 2.05 (m, 1H), 2.39 - 2.49 (m, 1H), 2.56 - 2.66 (m, 1H), 2.81 - 2.89 (m, 1H), 3.04 - 3.12 (m, 1H), 3.26 - 3.36 (m, 1H), 3.91 (s, 2H), 4.07 (s, 6H), 4.50 - 4.59 (m, 1H), 7.30 - 7.55 (m, 7H), 8.12 (d, J = 2.9 Hz, 1H), 8.60 (s, 1H), 8.73 (d, J = 9.3 Hz, 1H), 9.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 545 (M⁺+1)

Example 578: N-[(3S)-1-Benzyltetrahydro-1H-3-pyrrolyl]-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}urea

[0683] Chloroform (27 ml) and triethylamine (4 ml) were added to 4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitroaniline (200 mg) to prepare a solution. Triphosgene (192 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. (3S)-(+)-1-Benzyl-3-aminopyrrolidine (77 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (153 mg, yield 48%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.95 - 2.07 (m, 1H), 2.39 - 2.49 (m, 1H), 2.57 - 2.67 (m, 1H), 2.82 - 2.90 (m, 1H), 3.04 - 3.12 (m, 1H), 3.27 - 3.36 (m, 1H), 3.92 (s, 2H), 4.07 (s, 6H), 4.50 - 4.60 (m, 1H), 7.29 - 7.55 (m, 7H), 8.12 (d, J = 2.9 Hz, 1H), 8.60 (s, 1H), 8.73 (d, J = 9.5 Hz, 1H), 9.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 545 (M⁺+1)

Example 579: N-[1-(2-Chlorobenzyl)tetrahydro-1H-3-pyrrolyl]-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea

[0684] 3-Aminopyrrolidine (500 mg) was dissolved in acetonitrile (10 ml) to prepare a solution. 2-Chlorobenzyl bromide (0.75 ml), potassium carbonate (2.40 g) were added to the solution, and the mixture was stirred at room temperature for one hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform/methanol for development to give 1-(2-chlorobenzyl)-3-pyrrolidinamine (1) (453 mg, yield 37%).

[0685] Chloroform (10 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (100 mg) to prepare a solution. Triphosgene (110 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. The compound (1) (106 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (76 mg, yield 42%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.93 - 2.03 (m, 1H), 2.39 - 2.49 (m, 1H), 2.58 - 2.69 (m, 1H), 2.84 - 2.92 (m, 1H), 3.11 - 3.18 (m, 1H), 3.32 - 3.40 (m, 1H), 4.05 (s, 6H), 4.45 - 4.53 (m, 1H), 6.44 (d, J = 5.4 Hz, 1H), 7.05 - 7.12 (m, 2H), 7.27 - 7.34 (m, 2H), 7.38 - 7.47 (m, 4H), 7.54 - 7.64 (m, 2H), 8.46 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 533 (M⁺+1)

Example 580: N-[1-(2-Chlorobenzyl)tetrahydro-1H-3-pyrrolyl]-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}urea

[0686] Chloroform (10 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (100 mg) to prepare a solution. Triphosgene (110 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. 1-(2-Chlorobenzyl)-3-pyrrolidinamine (106 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (109 mg, yield 61%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.86 - 1.97 (m, 1H), 2.34 - 2.47 (m, 1H), 2.51 - 2.61 (m, 1H), 2.78 - 2.85 (m, 1H), 3.00 - 3.07 (m, 1H), 3.21 - 3.29 (m, 1H), 3.98 (s, 2H), 4.07 (s, 6H), 4.40 - 4.50 (m, 1H), 5.80 - 5.90 (m, 1H), 7.13 - 7.18 (m, 2H), 7.25 - 7.46 (m, 6H), 7.53 - 7.57 (m, 2H), 8.60 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 534 (M⁺+1)

Example 581: N-[1-(2-Chlorobenzyl)tetrahydro-1H-3-pyrrolyl]-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}urea

[0687] Chloroform (13 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitroaniline (100 mg) to prepare a solution. Triphosgene (96 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. 1-(2-Chlorobenzyl)-3-pyrrolidinamine (92 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (66 mg, yield 39%).

¹H-NMR (chloroform-d, 400 MHz): δ 2.05 - 2.16 (m, 1H), 2.40 - 2.50 (m, 1H), 2.60 - 2.69 (m, 1H), 2.87 - 2.93 (m, 1H), 3.03 - 3.10 (m, 1H), 3.25 - 3.33 (m, 1H), 4.04 (s, 2H), 4.07 (s, 6H), 4.51 - 4.60 (m, 1H), 7.26 - 7.56 (m, 5H), 7.62 - 7.68 (m, 1H), 8.12 (d, J = 2.7 Hz, 1H), 8.60 (s, 1H), 8.74 (d, J = 9.3 Hz, 1H), 9.79 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 579 (M⁺+1)

Example 582: N-[1-[4-(Tert-butyl)benzyl]tetrahydro-1H-3-pyrrolyl]-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea

[0688] 3-Aminopyrrolidine (500 mg) was dissolved in acetonitrile (10 ml) to prepare a solution. 4-(Tert-butyl)benzyl bromide (1.07 ml) and potassium carbonate (2.40 g) were added to the solution, and the mixture was stirred at room temperature for one hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform/methanol for development to give 1-[4-(tert-butyl)benzyl]-3-pyrrolidinamine (1) (589 mg, yield 44%).

[0689] Chloroform (10 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (100 mg) to prepare a solution. Triphosgene (110 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. (1) (117 mg) was then added thereto, and the mixture was stirred at room temperature for 5 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (71 mg, yield 38%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.32 (s, 9H), 2.12 - 2.28 (m, 1H), 2.43 - 2.55 (m, 1H), 2.83 - 2.93 (m, 1H), 3.01 - 3.09 (m, 1H), 3.38 - 3.45 (m, 1H), 3.62 - 3.72 (m, 1H), 4.04 (s, 3H), 4.04 (s, 3H), 4.11 (s, 1H), 4.13 (s, 1H), 4.61 - 4.70 (m, 1H), 6.43 (d, J = 5.4 Hz, 1H), 7.04 - 7.10 (m, 2H), 7.38 - 7.58 (m, 8H), 8.45 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 555 (M⁺+1)

Example 583: N-[1-[4-(Tert-butyl)benzyl]tetrahydro-1H-3-pyrrolyl]-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}urea

[0690] Chloroform (10 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (100 mg) to prepare a solution. Triphosgene (110 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. 1-[4-(Tert-butyl)benzyl]-3-pyrrolidinamine (117 mg) was then added thereto, and the mixture was stirred at room temperature for 5 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (76 mg, yield 41%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.31 (s, 9H), 2.07 - 2.12 (m, 1H), 2.37 - 2.48 (m, 1H), 2.57 - 2.66 (m, 1H), 2.78 - 2.88 (m, 1H), 3.11 - 3.19 (m, 1H), 3.32 - 3.42 (m, 1H), 3.89 (s, 1H), 3.91 (s, 1H), 4.06 (s, 6H), 4.44 - 4.55 (m, 1H), 7.12 - 7.17 (m, 2H), 7.28 - 7.57 (m, 8H), 8.60 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 556 (M⁺+1)

Example 584: N-[1-[4-(Tert-butyl)benzyl]tetrahydro-1H-3-pyrrolyl]-N'-{4-[(6,7-dimethoxy-4-quinazolinyloxy)-2-nitrophenyl]urea

[0691] Chloroform (13 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinazolinyloxy)-2-nitroaniline (100 mg) to prepare a solution. Triphosgene (96 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. 1-[4-(Tert-butyl)benzyl]-3-pyrrolidinamine (102 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (38 mg, yield 22%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.32 (s, 9H), 1.92 - 2.04 (m, 1H), 2.38 - 2.48 (m, 1H), 2.53 - 2.64 (m, 1H), 2.78 - 2.86 (m, 1H), 3.03 - 3.11 (m, 1H), 3.27 - 3.35 (m, 1H), 3.86 (s, 1H), 3.87 (s, 1H), 4.07 (s, 6H), 4.50 - 4.58 (m, 1H), 7.32 - 7.54 (m, 6H), 8.12 (d, J = 2.9 Hz, 1H), 8.60 (s, 1H), 8.71 - 8.75 (m, 1H), 9.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 601 (M⁺+1)

Example 585: N-[1-(Cyclohexylmethyl)tetrahydro-1H-3-pyrrolyl]-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea

[0692] 3-Aminopyrrolidine (500 mg) was dissolved in acetonitrile (10 ml) to prepare a solution. Cyclohexylmethyl bromide (0.81 ml), potassium carbonate (2.40 g), and tetra-n-butylammonium iodide (100 mg) were added to the solution, and the mixture was stirred at room temperature for 7 hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform/methanol for development to give 1-(cyclohexylmethyl)-3-pyrrolidinamine (1) (271 mg, yield 26%).

[0693] Chloroform (10 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (100 mg) to prepare a solution. Triphosgene (110 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. The compound (1) (74 mg) was then added thereto, and the mixture was stirred at room temperature for 3 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (85 mg, yield 50%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.00 - 1.32 (m, 6H), 1.64 - 1.85 (m, 4H), 1.91 - 2.03 (m, 2H), 2.27 - 2.38 (m, 1H), 2.48 - 2.60 (m, 1H), 2.88 - 2.98 (m, 2H), 3.65 - 3.73 (m, 1H), 4.04 (s, 6H), 4.05 (s, 2H), 4.68 - 4.78 (m, 1H), 6.44 (d, J = 5.4 Hz, 1H), 7.06 - 7.11 (m, 2H), 7.42 (s, 1H), 7.47 - 7.55 (m, 2H), 7.56 (s, 1H), 8.46 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 505 (M⁺+1)

Example 586: N-[1-(Cyclohexylmethyl)tetrahydro-1H-3-pyrrolyl]-N'-{4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}urea

[0694] Chloroform (10 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinazolinyloxy]aniline (100 mg) to prepare a solution. Triphosgene (110 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. 1-(Cyclohexylmethyl)-3-pyrrolidinamine (74 mg) was then added thereto, and the mixture was stirred at room temperature for 3 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (94 mg, yield 55%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.00 - 1.37 (m, 6H), 1.63 - 1.88 (m, 4H), 1.90 - 1.98 (m, 1H), 2.27 - 2.39 (m, 1H), 2.47 - 2.60 (m, 1H), 2.84 - 3.01 (m, 2H), 3.07 - 3.18 (m, 1H), 3.68 - 3.78 (m, 1H), 3.95 - 4.06 (m, 2H), 4.07 (s, 3H), 4.08 (s, 3H), 4.70 - 4.79 (m, 1H), 7.10 - 7.17 (m, 2H), 7.41 (s, 1H), 7.52 (s, 1H), 7.52 - 7.58 (m, 2H), 7.88 (s, 1H), 8.64 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 506 (M⁺+1)

Example 587: N-[1-(Cyclohexylmethyl)tetrahydro-1H-3-pyrrolyl]-N'-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl]urea

[0695] Chloroform (13 ml) and triethylamine (2 ml) were added to 4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitroaniline (100 mg) to prepare a solution. Triphosgene (96 mg) was added to the solution, and the mixture was stirred at room temperature for 30 min. 1-(Cyclohexylmethyl)-3-pyrrolidinamine (64 mg) was then added thereto, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (34 mg, yield 21%).

¹H-NMR (chloroform-d, 400 MHz): δ 0.94 - 1.34 (m, 6H), 1.61 - 1.81 (m, 4H), 1.87 - 1.99 (m, 2H), 2.06 - 2.20 (m, 1H), 2.40 - 2.52 (m, 1H), 2.61 - 2.73 (m, 2H), 2.83 - 2.93 (m, 1H), 3.28 - 3.40 (m, 1H), 3.52 - 3.63 (m, 1H), 4.07 (s, 6H), 4.57 - 4.68 (m, 1H), 7.33 (s, 1H), 7.51 (s, 2H), 8.12 (d, J = 2.9 Hz, 1H), 8.60 (s, 1H), 8.72 (d, J = 9.3 Hz, 1H), 9.82 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 551 (M⁺+1)

Example 588: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2-diethylaminopropyl)thiourea

[0696] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, N,N-diethylpropylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 14 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (25 mg, yield %).

¹H-NMR (CDCl₃, 400 MHz): 1.00 - 1.10 (m, 6H), 1.85 - 2.00 (m, 2H), 2.55 - 2.80 (m, 6H), 3.80 - 3.90 (m, 2H), 4.04 (s, 3H), 4.06 (s, 3H), 6.54 (d, J = 5.4 Hz, 1H), 7.19 (d, J = 6.8 Hz, 1H), 7.24 - 7.28 (m, 2H), 7.36 - 7.44 (m, 2H), 7.44 (s, 1H), 7.516 (s, 1H), 8.51 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 469 (M⁺+1)

Example 589: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2-diethylaminoethyl)thiourea

[0697] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in N,N-dimethylformamide (2 ml) and triethylamine (1 ml) to prepare a solution. Thiophosgene (51 mg) was then added to the solution, and the mixture was stirred at room temperature for 6 hr. Next, N,N-diethylethylenediamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for 14 hr. Ethyl acetate was added to the reaction solution, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (25 mg, yield 33%).

¹H-NMR (CDCl₃, 400 MHz): 0.90 - 1.10 (m, 6H), 2.45 - 2.75 (m, 2H), 3.60 - 3.75 (m, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 6.49 (s, 1H), 7.20 - 7.38 (m, 4H), 7.43 (s, 1H), 7.53 (s, 1H), 8.50 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 455 (M⁺+1)

Example 590: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-[4-(N-benzyl)piperidiny]urea

[0698] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-amino-1-benzylpiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (27 mg, yield 32%).

¹H-NMR (CDCl₃, 400 MHz): 1.45 - 1.55 (m, 2H), 1.95 - 2.05 (m, 2H), 2.13 - 2.23 (m, 2H), 2.80 - 2.90 (m, 2H), 3.52 (s, 2H), 3.70 - 3.80 (m, 1H), 4.04 (s, 6H), 4.85 - 4.95 (m, 1H), 6.44 (d, J = 5.4 Hz, 1H), 6.80 - 6.82 (m, 2H), 7.10 - 7.14 (m, 2H), 7.26 - 7.34 (m, 5H), 7.40 - 7.44 (m, 2H), 7.55 (s, 1H), 8.46 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 513 (M⁺+1)

Example 591: N-[4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl]-N'-(4-(N-benzyl)piperidinyl)urea

[0699] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-amino-1-benzylpiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (30 mg, yield 35%).

¹H-NMR (CDCl₃, 400 MHz): 1.45 - 1.60 (m, 2H), 1.95 - 2.05 (m, 2H), 2.15 - 2.25 (m, 2H), 2.80 - 2.90 (m, 2H), 3.55 (s, 2H), 3.70 - 3.80 (m, 1H), 4.07 (s, 6H), 4.70 - 4.80 (m, 1H), 4.47 (s, 1H), 7.19 (d, J = 9.2 Hz, 1H), 7.30 - 7.34 (m, 5H), 7.40 (d, J = 8.8 Hz, 2H), 7.55 (s, 1H), 8.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 514 (M⁺+1)

Example 592: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-(1-piperidinyl)urea

[0700] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-aminopiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (40 mg, yield 56%).

¹H-NMR (CDCl₃, 400 MHz): 1.60 - 1.85 (m, 6H), 2.33 - 2.46 (m, 2H), 3.15 - 3.25 (m, 2H), 4.057 (s, 3H), 4.059 (s, 3H), 5.33 (s, 1H), 6.45 (d, J = 5.4 Hz, 1H), 7.14 (d, J = 9.0 Hz, 2H), 7.45 (s, 1H), 7.57 - 7.62 (m, 3H), 8.23 (s, 1H), 8.47 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 423 (M⁺+1)

Example 593: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]-N'-(1-piperidinyl)urea

[0701] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-aminopiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (40 mg, yield 58%).

¹H-NMR (CDCl₃, 400 MHz): 1.50 - 1.90 (m, 6H), 2.12 (s, 3H), 2.25 (s, 3H), 2.35 - 2.50 (m, 2H), 3.15 - 3.25 (m, 2H), 4.07 (s, 3H), 4.08 (s, 3H), 5.41 (s, 1H), 6.30 (d, J = 5.6 Hz, 1H), 7.00 (d, J = 8.8 Hz, 1H), 7.53 (s, 1H), 7.64 (s, 1H), 7.84 (d, J = 8.8 Hz, 1H), 8.25 (s, 1H), 8.43 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 451 (M⁺+1)

Example 594: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-nitrophenyl]-N'-(1-piperidinyl)urea

[0702] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-nitroaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-aminopiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (35 mg, yield 51%).

¹H-NMR (CDCl₃, 400 MHz): 1.60 - 1.85 (m, 6H), 2.43 - 2.48 (m, 2H), 3.15 - 3.25 (m, 2H), 4.09 (s, 3H), 4.12 (s, 3H), 5.63 (s, 1H), 6.59 (d, J = 5.6 Hz, 1H), 7.47 - 7.52 (m, 1H), 7.57 (s, 1H), 7.82 (m, 1H), 8.12 (d, J = 2.9 Hz, 1H), 9.00 (d, J = 9.3 Hz, 1H), 11.42 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 468 (M⁺+1)

Example 595: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-chlorophenyl}-N'-(1-piperidinyl)urea

[0703] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-chloroaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-aminopiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (38 mg, yield 55%).

¹H-NMR (CDCl₃, 400 MHz): 1.60 - 1.85 (m, 6H), 2.35 - 2.50 (m, 2H), 3.15 - 3.25 (m, 2H), 4.07 (s, 6H), 5.45 - 5.50 (m, 1H), 7.15 - 7.19 (m, 1H), 7.34 - 7.36 (m, 2H), 7.53 (s, 1H), 8.44 - 8.47 (m, 1H), 8.63 (d, J = 1.2 Hz, 1H), 9.04 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 468 (M⁺+1)

Example 596: N-{4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-methoxyphenyl]-N'-(1-piperidinyl)urea

[0704] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-methoxyaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-aminopiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (45 mg, yield 65%).

¹H-NMR (CDCl₃, 400 MHz): 1.60 - 1.85 (m, 6H), 2.30 - 2.45 (m, 2H), 3.10 - 3.20 (m, 2H), 3.91 (s, 3H), 4.07 (s, 6H), 5.30 - 5.40 (m, 1H), 6.79 (d, J = 2.4 Hz, 1H), 6.82 - 6.86 (m, 1H), 7.33 (d, J = 2.2 Hz, 1H), 7.57 (d, J = 1.0 Hz, 1H), 8.33 (dd, J = 1.2 Hz, J = 8.5 Hz, 1H), 8.63 (d, J = 1.5 Hz, 1H), 8.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 454 (M⁺+1)

Example 597: N-{4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-nitrophenyl]-N'-(1-piperidinyl)urea

[0705] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-nitroaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-aminopiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (50 mg, yield 73%).

¹H-NMR (CDCl₃, 400 MHz): 1.50 - 2.00 (m, 6H), 2.38 - 2.48 (m, 2H), 3.15 - 3.20 (m, 2H), 4.08 (s, 3H), 4.09 (s, 3H), 5.57 (s, 1H), 7.36 (s, 1H), 7.53 - 7.57 (m, 2H), 8.17 (d, J = 2.9 Hz, 1H), 8.61 (s, 1H), 8.93 (d, J = 9.3 Hz, 1H), 11.41 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 469 (M⁺+1)

Example 598: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methoxyphenyl}-N'-(1-piperidinyl)urea

[0706] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methoxyaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-aminopiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (43 mg, yield 62%).

¹H-NMR (CDCl₃, 400 MHz): 1.50 - 1.80 (m, 6H), 2.30 - 2.45 (m, 2H), 3.15 - 3.25 (m, 2H), 3.89 (s, 3H), 4.07 (s, 6H), 5.33 (s, 1H), 6.50 (d, J = 5.6 Hz, 1H), 6.72 (d, J = 2.4 Hz, 1H), 6.80 (dd, J = 2.4 Hz, J = 8.8 Hz, 1H), 7.52 (s, 1H), 7.59 (s, 1H), 8.32 (d, J = 8.8 Hz, 1H), 8.47 (d, J = 5.4 Hz, 1H), 8.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 453 (M⁺+1)

Example 599: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-methoxyphenyl}-N'-(1-morphonyl)urea

[0707] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-methoxyaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-aminomorpholine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (26 mg, yield 37%).

¹H-NMR (CDCl₃, 400 MHz): 2.60 - 2.75 (m, 2H), 2.90 - 3.10 (m, 2H), 3.40 - 3.55 (m, 2H), 3.65 - 3.80 (m, 2H), 3.91 (s, 3H), 4.07 (s, 3H), 4.08 (s, 3H), 5.45 (s, 1H), 6.80 (d, J = 2.7 Hz, 1H), 6.85 (dd, J = 2.4 Hz, J = 8.8 Hz, 1H), 7.34 (s, 1H), 7.56 (s, 1H), 8.33 (d, J = 8.8 Hz, 1H), 8.63 (s, 1H), 8.73 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 456 (M⁺+1)

Example 600: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methoxyphenyl}-N'-(1-homopiperidinyl)urea

[0708] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methoxyaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-aminohomopiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (35 mg, yield 49%).

¹H-NMR (CDCl₃, 400 MHz): 1.50 - 1.90 (m, 8H), 2.85 - 3.00 (m, 2H), 3.05 - 3.20 (m, 2H), 3.90 (s, 3H), 4.07 (s, 3H), 4.08 (s, 3H), 5.66 (s, 1H), 6.75 - 6.90 (m, 2H), 7.32 (s, 1H), 7.57 (s, 1H), 8.35 (d, J = 8.5 Hz, 1H), 8.63 (s, 1H), 8.95 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 468 (M⁺+1)

Example 601: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(1-morphonyl)urea

[0709] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-aminomorpholine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (47 mg, yield 66%).

¹H-NMR (CDCl₃, 400 MHz): 2.50 - 2.70 (m, 2H), 2.90 - 3.10 (m, 2H), 3.65 - 3.85 (m, 2H), 3.85 - 4.00 (m, 2H), 4.07 (s, 3H), 4.08 (s, 3H), 5.45 (s, 1H), 7.21 (d, J = 9.0 Hz, 2H), 7.33 (s, 1H), 7.56 (s, 1H), 7.60 (d, J = 9.0 Hz, 2H), 8.12 (s, 1H), 8.61 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 426 (M⁺+1)

Example 602: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(1-homopiperidinyl)urea

[0710] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-aminohomopiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted

with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (48 mg, yield 65%).

¹H-NMR (CDCl₃, 400 MHz): 1.55 - 1.85 (m, 8H), 2.85 - 3.00 (m, 2H), 3.05 - 3.20 (m, 2H), 4.07 (s, 3H), 4.08 (s, 3H), 5.67 (s, 1H), 7.19 (d, J = 9.0 Hz, 2H), 7.33 (s, 1H), 7.57 (s, 1H), 7.60 (d, J = 8.8 Hz, 2H), 8.33 (s, 1H), 8.62 (s, 1H)
Mass spectrometry value (ESI-MS, m/z): 438 (M⁺+1)

Example 603: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(1-piperidinyl)urea

[0711] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-aminopiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (47 mg, yield 66%).

¹H-NMR (CDCl₃, 400 MHz): 1.50 - 1.80 (m, 6H), 2.30 - 2.45 (m, 2H), 3.10 - 3.20 (m, 2H), 4.07 (s, 3H), 4.08 (s, 3H), 5.40 - 5.50 (m, 1H), 7.19 (d, J = 8.8 Hz, 2H), 7.35 (s, 1H), 7.57 (s, 1H), 7.59 (d, J = 8.8 Hz, 2H), 8.25 (s, 1H), 8.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 424 (M⁺+1)

Example 604: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}-N'-[4-(N-benzyl)piperidinyl]urea

[0712] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-amino-1-benzylpiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (45 mg, yield 55%).

¹H-NMR (CDCl₃, 400 MHz): 2.07 - 2.18 (m, 4H), 2.24 (s, 3H), 2.40 - 2.54 (m, 1H), 2.80 - 2.95 (m, 1H), 3.25 - 3.30 (m, 1H), 3.45 - 3.60 (m, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 4.09 (d, J = 12.7 Hz, 1H), 4.14 (d, J = 12.7 Hz, 1H), 4.60 (s, 1H), 6.30 (d, J = 5.4 Hz, 1H), 6.90 - 7.00 (m, 2H), 7.10 - 7.54 (m, 7H), 7.61 (s, 1H), 8.63 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 527 (M⁺+1)

Example 605: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-chlorophenyl}-N'-[4-(N-benzyl)piperidinyl]urea

[0713] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-chloroaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-amino-1-benzylpiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (35 mg, yield 43%).

¹H-NMR (CDCl₃, 400 MHz): 1.73 - 1.80 (m, 2H), 2.25 - 2.40 (m, 2H), 2.56 - 2.63 (m, 1H), 2.71 - 2.76 (m, 1H), 2.98 - 3.00 (m, 1H), 3.62 (d, J = 12.7 Hz, 1H), 3.66 (d, J = 12.9 Hz, 1H), 4.07 (s, 6H), 4.30 - 4.40 (m, 1H), 5.30 (br, 1H), 7.14 - 7.18 (m, 1H), 7.30 - 7.33 (m, 7H), 7.52 (s, 1H), 8.17 - 8.22 (m, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 534 (M⁺+1)

Example 606: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}-N'-[4-(N-benzyl)piperidinyl]urea

[0714] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-nitroaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-amino-1-benzylpiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous

sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (45 mg, yield 57%).

¹H-NMR (CDCl₃, 400 MHz): 1.75 - 1.80 (m, 2H), 2.32 - 2.43 (m, 2H), 2.62 - 2.68 (m, 1H), 2.73 - 2.78 (m, 1H), 2.95 - 3.01 (m, 1H), 3.68 (s, 2H), 4.07 (s, 3H), 4.08 (s, 3H), 4.41 (s, 1H), 5.48 (s, 1H), 7.27 - 7.36 (m, 6H), 7.50 - 7.55 (m, 2H), 8.13 (d, J = 2.7 Hz, 1H), 8.60 (s, 1H), 8.77 (d, J = 9.3 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 545 (M⁺+1)

Example 607: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methoxyphenyl}-N'-(4-(N-benzyl)piperidinyl)urea

[0715] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methoxyaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 4-amino-1-benzylpiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (55 mg, yield 68%).

¹H-NMR (CDCl₃, 400 MHz): 1.80 - 1.90 (m, 1H), 2.35 - 2.50 (m, 2H), 2.70 - 2.75 (m, 1H), 2.88 - 2.93 (m, 1H), 3.09 - 3.16 (m, 1H), 3.23 - 3.31 (m, 1H), 3.75 (d, J = 12.9 Hz, 1H), 3.79 (d, J = 12.9 Hz, 1H), 3.84 (s, 3H), 4.07 (s, 6H), 4.45 - 4.55 (m, 1H), 5.67 (d, J = 7.6 Hz, 1H), 6.77 (d, J = 2.4 Hz, 1H), 6.82 (dd, J = 2.4 Hz, J = 8.8 Hz, 1H), 6.92 (s, 1H), 7.30 - 7.40 (m, 5H), 7.55 (s, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 530 (M⁺+1)

Example 608: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(1-homopiperidinyl)urea

[0716] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-aminohomopiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (35 mg, yield 47%).

¹H-NMR (CDCl₃, 400 MHz) : ¹H-NMR (CDCl₃, 400 MHz) : 1.50 - 1.80 (m, 8H), 2.85 - 3.00 (m, 2H), 3.10 - 3.20 (m, 2H), 4.055 (s, 3H), 4.059 (s, 3H), 5.66 (s, 1H), 6.45 (d, J = 5.4 Hz, 1H), 7.14 (d, J = 6.8 Hz, 2H), 7.44 (s, 1H), 7.58 (s, 1H), 7.59 (d, J = 6.8 Hz, 2H), 8.32 (s, 1H), 8.47 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 437 (M⁺+1)

Example 609: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-(1-homopiperidinyl)urea

[0717] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-aminohomopiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (43 mg, yield 55%).

¹H-NMR (CDCl₃, 400 MHz): 1.55 - 1.85 (m, 8H), 2.85 - 3.00 (m, 2H), 3.10 - 3.20 (m, 2H), 4.07 (s, 3H), 4.09 (s, 3H), 5.80 (s, 1H), 6.55 (d, J = 5.6 Hz, 1H), 6.98 - 7.03 (m, 2H), 7.55 (s, 1H), 7.65 (s, 1H), 8.37 - 8.43 (m, 1H), 8.50 (d, J = 5.9 Hz, 1H), 8.65 - 8.70 (m, 1H)

Mass spectrometry value (ESI-MS, m/z): 491 (M⁺+1)

Example 610: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-(1-pyrrolidinyl)urea

[0718] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5

ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-aminopyrrolidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (47 mg, yield 69%).

¹H-NMR (CDCl₃, 400 MHz): 1.86 - 2.00 (m, 4H), 2.50 - 2.70 (m, 2H), 2.85 - 3.05 (m, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 6.05 (s, 1H), 6.50 (d, J = 5.4 Hz, 1H), 6.95 - 7.05 (m, 2H), 7.45 (s, 1H), 7.53 (s, 1H), 8.30 - 8.35 (m, 1H), 8.45 - 8.55 (m, 2H)

Mass spectrometry value (ESI-MS, m/z): 463 (M⁺+1)

Example 611: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-(methylamino)urea

[0719] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, methylhydrazine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (47 mg, yield 76%).

¹H-NMR (CDCl₃, 400 MHz): 3.18 (s, 3H), 4.06 (s, 3H), 4.08 (s, 3H), 6.55 (d, J = 8.5 Hz, 1H), 7.53 (s, 1H), 7.60 (s, 1H), 8.05 (s, 1H), 8.37 (t, J = 9.3 Hz, 1H), 8.49 (d, J = 5.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 423 (M⁺+1)

Example 612: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-(phenylamino)urea

[0720] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, phenylhydrazine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (47 mg, yield 66%).

¹H-NMR (CDCl₃, 400 MHz): 4.06 (s, 3H), 4.08 (s, 3H), 5.95 (s, 1H), 6.36 (s, 1H), 6.55 (d, J = 5.6 Hz, 1H), 6.94 - 7.07 (m, 5H), 7.30 - 7.36 (m, 2H), 7.53 (s, 1H), 7.62 (s, 1H), 8.15 - 8.20 (m, 1H), 8.38 (d, J = 9.0 Hz, 1H), 8.49 (d, J = 5.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 485 (M⁺+1)

Example 613: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-(1-piperidinyl)urea

[0721] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was added to toluene (5 ml), and triethylamine (0.5 ml), and the mixture was heated under reflux to prepare a solution. A solution of triphosgene (50 mg) in methylene chloride was then added thereto, and the mixture was heated under reflux for 10 min. Next, 1-aminopiperidine (50 mg) was added thereto, and the mixture was further stirred with heating under reflux for 3 hr. A saturated aqueous sodium bicarbonate solution was added to the reaction solution to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with water and saturated brine in that order. The organic layer was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by HPLC using chloroform/methanol for development to give the title compound (43 mg, yield 61%).

¹H-NMR (CDCl₃, 400 MHz): 1.60 - 1.90 (m, 6H), 2.35 - 2.50 (m, 2H), 3.15 - 3.25 (m, 2H), 4.06 (s, 3H), 4.08 (s, 3H), 5.49 (s, 1H), 6.54 (d, J = 5.6 Hz, 1H), 6.96 - 7.03 (m, 2H), 7.55 (s, 1H), 7.61 (s, 1H), 8.35 - 8.40 (m, 1H), 8.50 (d, J = 5.6 Hz, 1H), 8.53 - 8.56 (m, 1H)

Mass spectrometry value (ESI-MS, m/z): 477 (M⁺+1)

Example 614: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-methylbenzoyl)thiourea

[0722] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml), and ethanol (1 ml) to prepare a solution. Commercially available 2-methyl-1-benzenecarbonyl isothiocyanate (50 μ l) was then added thereto, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (78 mg, yield 97%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.17 (s, 3H), 4.09 (s, 3H), 4.13 (s, 3H), 6.69 (d, J = 5.86 Hz, 1H), 7.26 - 7.36 (m, 5H), 7.47 - 7.49 (m, 1H), 7.58 (d, J = 8.05 Hz, 1H), 7.61 (s, 1H), 7.88 (bs, 1H), 7.94 (d, J = 9.03 Hz, 2H), 8.52 (d, J = 5.86 Hz, 1H), 8.89 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 474 (M⁺+1)

Example 615: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}-N'-(2-phenylacetyl)thiourea

[0723] According to the description of technical literature, commercially available 2-phenylethanoyl chloride (80 mg) was dissolved in acetonitrile (20 ml). Potassium thiocyanate (300 mg) was added to the solution, and the mixture was heated at 80°C for 2 hr. Water was added to the reaction solution, and the organic layer was extracted and was concentrated to give 2-phenylethanoyl isothiocyanate. 2-Phenylethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (66 mg, yield 85%) (Referenc: Elmore, D.T. et al., Journal of chemical Society 1956, 4458).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.84 (s, 2H), 3.94 (s, 3H), 3.95 (s, 3H), 6.50 (d, J = 5.37 Hz, 1H), 7.27 - 7.55 (m, 9H), 8.01 (dd, J = 2.07 Hz, J = 12.32 Hz, 1H), 8.51 (d, J = 5.37 Hz, 1H), 11.82 (s, 1H), 2.49 (s, 1H) Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

[0724] In the following examples, when carbonyl isothiocyanate is used, except for the case where the carbonyl isothiocyanate is purchasable, this compound was prepared from a fatty acid or an acid chloride by the method described in Example 615 according to the method of the literature and was used in the reaction without isolation and purification

Example 616: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}-N'-(2-morpholinoethyl)urea

[0725] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was dissolved in chloroform (5 ml), and triethylamine (0.5 ml) to prepare a solution. A solution of triphosgene (68 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-morpholino-1-ethanamine (30 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (70 mg, yield 84%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.15 (s, 3H), 2.26 (s, 3H), 2.47 (s, 4H), 2.52 - 2.55 (m, 2H), 3.38 - 3.42 (m, 2H), 3.63 - 3.66 (m, 4H), 4.05 (s, 3H), 4.07 (s, 3H), 5.43 - 5.45 (m, 1H), 6.30 (d, J = 5.4 Hz, 1H), 6.49 (s, 1H), 6.97 (s, 1H), 7.43 (s, 1H), 7.47 (s, 1H), 7.59 (s, 1H), 8.45 (d, J = 5.1 Hz, 1H)

Example 617: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}-N'-(2-morpholinoethyl)urea

[0726] 4-[(6,7-Dimethyl-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was dissolved in chloroform (5 ml), and triethylamine (0.5 ml) to prepare a solution. A solution of triphosgene (68 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-morpholino-1-ethanamine (30 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (90 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.14 (s, 3H), 2.28 (s, 3H), 2.48 - 2.53 (m, 6H), 3.24 - 3.41 (m, 2H), 3.62 - 3.64 (m, 4H), 4.06 (s, 3H), 4.07 (s, 3H), 5.31 - 5.32 (m, 1H), 6.26 (d, J = 5.4 Hz, 1H), 6.49 (s, 1H), 7.01 (d, J = 8.5 Hz, 1H), 7.32 (d, J = 8.5 Hz, 1H), 7.44 (s, 1H), 7.61 (s, 1H), 8.45 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 481 (M⁺+1)

Example 618: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2-tetrahydro-1H-1-pyrrolylethyl)urea

[0727] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in chloroform (5 ml), and triethylamine (0.5 ml) to prepare a solution. A solution of triphosgene (77 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-tetrahydro-1H-1-pyrrolyl-1-ethanamine (30 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (40 mg, yield 46%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.82 - 1.90 (m, 4H), 2.68 - 2.85 (m, 6H), 3.38 - 3.46 (m, 2H), 4.05 (s, 6H), 5.35 (s, 1H), 5.97 (s, 1H), 6.44 (d, J = 5.4 Hz, 1H), 7.09 (d, J = 8.8 Hz, 2H), 7.41 (s, 1H), 7.48 (d, J = 8.8 Hz, 2H), 7.57 (s, 1H), 8.46 (d, J = 5.4 Hz, 1H)

Example 619: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]-N'-(2-tetrahydro-1H-1-pyrrolylethyl)urea

[0728] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was dissolved in chloroform (5 ml), and triethylamine (0.5 ml) to prepare a solution. A solution of triphosgene (68 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-tetrahydro-1H-1-pyrrolyl-1-ethanamine (26 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (26 mg, yield 32%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.86 (s, 4H), 2.13 (s, 3H), 2.26 (s, 3H), 2.70 - 2.77 (m, 4H), 2.81 (t, J = 5.6 Hz, 2H), 3.45 - 3.49 (m, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 5.89 (s, 1H), 6.30 (d, J = 5.1 Hz, 1H), 6.93 (s, 1H), 7.42 (s, 1H), 7.55 (s, 1H), 7.59 (s, 1H), 8.44 (d, J = 5.1 Hz, 1H)

Example 620: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]-N'-(2-tetrahydro-1H-1-pyrrolylethyl)urea

[0729] 4-[(6,7-Dimethyl-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was dissolved in chloroform (5 ml), and triethylamine (0.5 ml) to prepare a solution. A solution of triphosgene (68 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-tetrahydro-1H-1-pyrrolyl-1-ethanamine (26 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (21 mg, yield 26%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.86 (s, 4H), 2.11 (s, 3H), 2.27 (s, 3H), 2.76 (s, 4H), 2.82 (t, J = 5.6 Hz, 2H), 3.42 - 3.49 (m, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 5.86 (s, 1H), 6.27 (d, J = 5.1 Hz, 1H), 6.97 (d, J = 8.8 Hz, 1H), 7.39 (d, J = 8.8 Hz, 1H), 7.43 (s, 1H), 7.61 (s, 1H), 8.43 (d, J = 5.1 Hz, 1H)

Example 621: N-[4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl]-N'-(2-tetrahydro-1H-1-pyrrolylethyl)urea

[0730] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in chloroform (5 ml), and triethylamine (0.5 ml) to prepare a solution. A solution of triphosgene (77 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-tetrahydro-1H-1-pyrrolyl-1-ethanamine (30 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (8 mg, yield 9%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.86 (s, 4H), 2.72 - 2.92 (m, 6H), 3.39 - 3.45 (m, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 5.42 (s, 1H), 7.16 (d, J = 9.0 Hz, 2H), 7.31 (s, 1H), 7.48 (d, J = 8.8 Hz, 2H), 7.56 (s, 1H), 8.61 (s, 1H)

Example 622: N-[2-(Diethylamino)ethyl]-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]urea

[0731] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in chloroform (5 ml), and triethylamine (0.5 ml) to prepare a solution. A solution of triphosgene (77 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diethyl-1,2-ethanediamine (30 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (10 mg, yield 13%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.12 (t, J = 7.1 Hz, 6H), 2.66 - 2.71 (m, 6H), 3.35 - 3.36 (m, 2H), 4.05 (s, 6H), 6.46 (d, J = 5.4 Hz, 1H), 7.10 - 7.13 (m, 2H), 7.42 (s, 1H), 7.45 (d, J = 9.0 Hz, 2H), 7.57 (s, 1H), 8.47 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 439 (M⁺+1)

Example 623: N-[2-(Diethylamino)ethyl]-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]urea

[0732] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was dissolved in chloroform (5 ml), and triethylamine (0.5 ml) to prepare a solution. A solution of triphosgene (68 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diethyl-1,2-ethanediamine (27 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (7 mg, yield 10%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.12 (t, J = 7.1 Hz, 6H), 2.13 (s, 3H), 2.27 (s, 3H), 2.70 - 2.77 (m, 6H), 3.43 - 3.45 (m, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 6.30 (d, J = 5.4 Hz, 1H), 6.95 (s, 1H), 7.42 (s, 1H), 7.49 (s, 1H), 7.59 (s, 1H), 8.44 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 467 (M⁺+1)

Example 624: N-[2-(Diethylamino)ethyl]-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]urea

[0733] 4-[(6,7-Dimethyl-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was dissolved in chloroform (5 ml), and triethylamine (0.5 ml) to prepare a solution. A solution of triphosgene (68 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diethyl-1,2-ethanediamine (27 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (8 mg, yield 11%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.03 (t, J = 7.1 Hz, 6H), 2.12 (s, 3H), 2.28 (s, 3H), 2.58 - 2.67 (m, 6H), 3.35 - 3.38 (m, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 6.26 (d, J = 5.4 Hz, 1H), 6.98 (d, J = 8.8 Hz, 1H), 7.32 (d, J = 8.8 Hz, 1H), 7.43 (s, 1H), 7.61 (s, 1H), 8.43 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 467 (M⁺+1)

Example 625: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]-N'-[2-(dimethylamino)ethyl]urea

[0734] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (50 mg) was dissolved in chloroform (5 ml), and triethylamine (0.5 ml) to prepare a solution. A solution of triphosgene (68 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-dimethyl-1,2-ethanediamine (20 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (24 mg, yield 36%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.03 (s, 3H), 2.13 (s, 3H), 2.25 (s, 3H), 2.28 (s, 3H), 2.51 (s, 2H), 3.38 - 3.39 (m, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 5.59 (s, 1H), 6.30 (d, J = 4.9 Hz, 1H), 6.94 (s, 1H), 7.42 (s, 1H), 7.55 (s, 1H), 7.59 (s, 1H), 8.44 (d, J = 5.1 Hz, 1H)

Example 626: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]-N'-[2-(dimethylamino)ethyl]urea

[0735] 4-[(6,7-Dimethyl-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was dissolved in chloroform (5 ml), and triethylamine (0.5 ml) to prepare a solution. A solution of triphosgene (68 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-dimethyl-1,2-ethanediamine (20 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (18 mg, yield 28%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.02 (s, 3H), 2.12 (s, 3H), 2.26 (s, 6H), 2.44 - 2.51 (m, 2H), 3.37 - 3.38 (m, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 5.45 (s, 1H), 6.26 (d, J = 5.1 Hz, 1H), 6.99 (d, J = 8.8 Hz, 1H), 7.38 (d, J = 8.3 Hz, 1H), 7.43 (s, 1H), 7.61 (s, 1H), 8.44 (d, J = 5.1 Hz, 1H)

Example 627: N-[4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl]-N'-[2-(dimethylamino)ethyl]urea

[0736] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in chloroform (5 ml), and triethylamine (0.5 ml) to prepare a solution. A solution of triphosgene (77 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-dimethyl-1,2-ethanediamine (23 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (14 mg, yield 21%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.27 (s, 3H), 2.34 (s, 3H), 2.46 - 2.49 (m, 2H), 3.31 - 3.35 (m, 2H), 4.07 (s, 6H), 5.14 (s, 1H), 5.59 (s, 1H), 7.16 (d, J = 8.3 Hz, 2H), 7.31 (s, 1H), 7.47 (d, J = 8.5 Hz, 2H), 7.56 (s, 1H), 8.61 (s, 1H)

Example 628: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2-morpholinoethyl)urea

[0737] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (100 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-morpholino-1-ethanamine (66 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (162 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.46 - 2.48 (m, 4H), 2.54 (t, J = 5.9 Hz, 2H), 3.40 (q, J = 5.4 Hz, 2H), 3.64 (t, J = 4.6 Hz, 4H), 4.03 (s, 3H), 4.05 (s, 3H), 5.59 (s, 1H), 6.45 (d, J = 5.4 Hz, 1H), 7.12 (d, J = 8.8 Hz, 2H), 7.41 (s, 1H), 7.47 (d, J = 8.8 Hz, 2H), 7.57 (s, 1H), 8.47 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 453 (M⁺+1)

Example 629: N-[4-[(6,7-Dimethoxy-4-quinazolinyloxy]phenyl]-N'-(2-morpholinoethyl)urea

[0738] 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (100 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-morpholino-1-ethanamine (66 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (41 mg, yield 27%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.45 (t, J = 4.1 Hz, 4H), 2.51 (t, J = 5.6 Hz, 2H), 3.38 (q, J = 5.6 Hz, 2H), 3.63 (t, J = 4.6 Hz, 4H), 4.06 (s, 3H), 4.07 (s, 3H), 5.66 (t, J = 5.1 Hz, 1H), 7.17 (d, J = 8.8 Hz, 2H), 7.31 (s, 1H), 7.44 (d, J = 8.8 Hz, 2H), 7.55 (s, 1H), 7.64 (s, 1H), 8.60 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 454 (M⁺+1)

Example 630: N-[2-(Diethylamino)ethyl]-N'-[4-[(6,7-dimethoxy-4-quinazolinyloxy]-2-methoxyphenyl]urea

[0739] 4-[(6,7-Dimethoxy-4-quinazolinyloxy]-2-methoxyaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (140 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diethyl-1,2-ethanediamine (55 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (83 mg, yield 57%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.39 (t, J = 7.3 Hz, 6H), 3.11 - 3.20 (m, 6H), 3.65 - 3.68 (m, 2H), 3.85 (s, 3H), 4.065 (s, 3H), 4.067 (s, 3H), 6.77 - 6.82 (m, 2H), 7.30 (s, 1H), 7.54 (s, 1H), 7.62 (s, 1H), 8.16 (d, J = 8.8 Hz, 1H), 8.61 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 470 (M⁺+1)

Example 631: N-[4-[(6,7-Dimethoxy-4-quinazolinyloxy]-2-methoxyphenyl]-N'-(2-morpholinoethyl)urea

[0740] 4-[(6,7-Dimethoxy-4-quinazolinyloxy]-2-methoxyaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (140 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-morpholino-1-ethanamine (61 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (165 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.49 - 2.57 (m, 6H), 3.39 - 3.43 (m, 2H), 3.70 - 3.73 (m, 4H), 3.84 (s, 3H), 4.068 (s, 3H), 4.072 (s, 3H), 5.53 (s, 1H), 6.79 - 6.86 (m, 2H), 6.97 - 6.98 (m, 1H), 7.33 (s, 1H), 7.55 (s, 1H), 8.14 (d, J = 8.8 Hz, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 484 (M⁺+1)

Example 632: N-[4-[(6,7-Dimethoxy-4-quinazolinyloxy]-2-methoxyphenyl]-N'-(2-tetrahydro-1H-1-pyrrolylethyl)urea

[0741] 4-[(6,7-Dimethoxy-4-quinazolinyloxy]-2-methoxyaniline (100 mg) was dissolved in chloroform (10 ml) and

triethylamine (1 ml) to prepare a solution. A solution of triphosgene (140 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-tetrahydro-1H-1-pyrrolyl-1-ethanamine (54 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.16 - 2.19 (m, 4H), 3.08 - 3.14 (m, 4H), 3.31 - 3.34 (m, 2H), 3.70 - 3.74 (m, 2H), 3.87 (s, 3H), 4.065 (s, 3H), 4.068 (s, 3H), 6.76 - 6.81 (m, 2H), 7.31 (s, 1H), 7.36 (s, 1H), 7.55 (s, 1H), 7.59 (s, 1H), 8.19 (d, J = 8.5 Hz, 1H), 8.62 (s, 1H)

Example 633: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-methoxyphenyl}-N'-[3-(4-methylpiperazino)propyl]urea

[0742] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-methoxyaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (140 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 3-(4-methylpiperazino)-1-propanamine (74 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (62 mg, yield 39%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.70 - 1.75 (m, 2H), 2.29 (d, J = 7.6 Hz, 3H), 2.41 - 2.52 (m, 10H), 3.24 - 3.46 (m, 2H), 3.84 (d, J = 4.4 Hz, 3H), 4.07 (s, 6H), 6.77 - 6.85 (m, 3H), 7.32 (d, J = 1.7 Hz, 1H), 7.55 (s, 1H), 8.18 (d, J = 8.8 Hz, 1H), 8.63 (s, 1H)

Example 634: N-(1-Benzyl-4-piperidyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}urea

[0743] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (140 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 1-benzyl-4-piperidineamine (89 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (124 mg, yield 74%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.43 - 1.51 (m, 2H), 1.97 - 1.99 (m, 4H), 2.14 (s, 3H), 2.21 (s, 3H), 2.82 - 2.84 (m, 2H), 3.50 (s, 2H), 4.047 (s, 3H), 4.053 (s, 3H), 4.95 (d, J = 7.8 Hz, 1H), 6.30 (d, J = 5.4 Hz, 1H), 6.35 (s, 1H), 6.94 (s, 1H), 7.27 - 7.31 (m, 5H), 7.43 (s, 1H), 7.51 (s, 1H), 7.59 (s, 1H), 8.45 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 541 (M⁺+1)

Example 635: N-(1-Benzyl-4-piperidyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}urea

[0744] 4-[(6,7-Dimethyl-4-quinolyl)oxy]-2,3-dimethylaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 1-benzyl-4-piperidineamine (89 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (101 mg, yield 60%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.41 - 1.44 (m, 2H), 1.95 - 1.97 (m, 4H), 2.13 (s, 3H), 2.25 (s, 3H), 2.81 (d, J = 11.7 Hz, 2H), 3.49 (s, 2H), 3.71 - 3.75 (m, 1H), 4.05 (s, 3H), 4.06 (s, 3H), 6.26 (d, J = 5.4 Hz, 1H), 6.99 (d, J = 8.5 Hz, 1H), 7.26 - 7.32 (m, 7H), 7.44 (s, 1H), 7.61 (s, 1H), 8.45 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 541 (M⁺+1)

Example 636: N-(1-Benzyl-4-piperidyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}urea

[0745] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (151 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 1-benzyl-4-piperidineamine (97 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (142 mg, yield 81%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.41 - 1.51 (m, 2H), 1.94 - 1.96 (m, 2H), 2.07 - 2.16 (m, 2H), 2.79 - 2.82 (m, 2H), 3.48 (s, 2H), 3.68 - 3.75 (m, 1H), 4.05 (s, 6H), 5.09 (d, J = 7.8 Hz, 1H), 7.07 (s, 1H), 7.16 (d, J = 9.0 Hz, 2H), 7.26 - 7.31 (m, 5H), 7.40 (d, J = 9.0 Hz, 2H), 7.54 (s, 1H), 8.59 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 514 (M⁺+1)

Example 637: N-(1-Benzyl-4-piperidyl)-N'-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}urea

[0746] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (134 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 1-benzyl-4-piperidineamine (85 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (185 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.40 - 1.55 (m, 2H), 1.93 - 1.99 (m, 2H), 2.12 - 2.17 (m, 2H), 2.81 - 2.83 (m, 2H), 3.49 (s, 2H), 3.70 - 3.74 (m, 1H), 4.05 (s, 3H), 4.06 (s, 3H), 5.74 (d, J = 7.8 Hz, 1H), 7.13 - 7.16 (m, 1H), 7.23 - 7.32 (m, 7H), 7.51 (s, 1H), 8.29 (d, J = 9.0 Hz, 1H), 8.61 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 548 (M⁺+1)

Example 638: N-(1-Benzyl-4-piperidyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-nitrophenyl}urea

[0747] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-nitroaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (131 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 1-benzyl-4-piperidineamine (84 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (141 mg, yield 86%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.55 - 1.63 (m, 2H), 1.97 - 2.03 (m, 4H), 2.81 - 2.90 (m, 2H), 3.53 (s, 2H), 3.72 - 3.73 (m, 1H), 4.04 (s, 3H), 4.05 (s, 3H), 5.35 - 5.36 (m, 1H), 6.47 (d, J = 5.1 Hz, 1H), 7.26 - 7.50 (m, 7H), 8.01 (d, J = 2.9 Hz, 1H), 8.52 (d, J = 5.4 Hz, 1H), 8.77 (d, J = 9.3 Hz, 1H), 9.72 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 558 (M⁺+1)

Example 639: N-(1-Benzyl-4-piperidyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}urea

[0748] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (142 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 1-benzyl-4-piperidineamine (91 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (47 mg, yield 28%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.47 - 1.55 (m, 2H), 1.98 - 2.00 (m, 2H), 2.15 - 2.20 (m, 2H), 2.84 - 2.87 (m, 2H), 3.53 (s, 2H), 3.70 - 3.80 (m, 1H), 4.04 (s, 3H), 4.05 (s, 3H), 4.89 (d, J = 7.3 Hz, 1H), 6.40 (d, J = 5.1 Hz, 1H), 6.93 (s, 1H), 7.06 - 7.17 (m, 2H), 7.26 - 7.32 (m, 5H), 7.41 (s, 1H), 7.49 - 7.53 (m, 1H), 7.58 (s, 1H), 8.47 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 531 (M⁺+1)

Example 640: N-(1-Benzyl-4-piperidyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}urea

[0749] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-nitroaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (131 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 1-benzyl-4-piperidineamine (89 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (151 mg, yield 93%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.54 - 1.63 (m, 2H), 2.01 - 2.03 (m, 2H), 2.16 - 2.21 (m, 2H), 2.87 - 2.90 (m, 2H), 3.54 (s, 2H), 3.72 - 3.73 (m, 1H), 4.07 (s, 3H), 4.08 (s, 3H), 4.97 (brs, 1H), 7.26 - 7.34 (m, 5H), 7.51 - 7.56 (m, 2H), 8.13 (d, J = 2.9 Hz, 1H), 8.60 (s, 1H), 8.80 (d, J = 9.5 Hz, 1H), 9.77 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 559 (M⁺+1)

Example 641: N-(1-Benzyl-4-piperidyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-methoxyphenyl}urea

[0750] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-methoxyaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the

solution, and the mixture was stirred at room temperature for 10 min. Next, 1-benzyl-4-piperidineamine (89 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (118 mg, yield 71%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.47 - 1.54 (m, 2H), 1.98 - 2.01 (m, 2H), 2.13 - 2.19 (m, 2H), 2.83 - 2.86 (m, 2H), 3.52 (s, 2H), 3.70 - 3.73 (m, 1H), 3.85 (s, 3H), 4.07 (s, 6H), 4.66 (d, J = 8.1 Hz, 1H), 6.71 (s, 1H), 6.78 (d, J = 2.4 Hz, 1H), 6.82 - 6.85 (m, 1H), 7.26 - 7.52 (m, 5H), 7.55 (s, 1H), 8.10 (d, J = 8.8 Hz, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 544 (M⁺+1)

Example 642: N-(1-Benzyl-4-piperidyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-methylphenyl}urea

[0751] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (142 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 1-benzyl-4-piperidineamine (91 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (84 mg, yield 50%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.46 - 1.54 (m, 2H), 1.97 - 2.00 (m, 2H), 2.13 (s, 3H), 2.13 - 2.23 (m, 2H), 2.82 - 2.85 (m, 2H), 3.51 (s, 2H), 3.73 - 3.75 (m, 1H), 4.04 (s, 3H), 4.05 (s, 3H), 4.98 (d, J = 7.8 Hz, 1H), 6.27 (d, J = 5.4 Hz, 1H), 6.90 (s, 1H), 7.02 (d, J = 8.5 Hz, 1H), 7.18 - 7.21 (m, 1H), 7.25 - 7.31 (m, 4H), 7.36 (d, J = 2.4 Hz, 1H), 7.42 (s, 1H), 7.60 (s, 1H), 8.43 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 527 (M⁺+1)

Example 643: N-(1-Benzyl-4-piperidyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-methylphenyl}urea

[0752] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (142 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 1-benzyl-4-piperidineamine (91 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (88 mg, yield 52%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.42 - 1.50 (m, 2H), 1.96 - 1.98 (m, 2H), 2.12 - 2.18 (m, 2H), 2.28 (s, 3H), 2.81 - 2.84 (m, 2H), 3.50 (s, 2H), 3.73 - 3.75 (m, 1H), 4.04 (s, 3H), 4.05 (s, 3H), 4.68 (d, J = 7.6 Hz, 1H), 6.15 (s, 1H), 6.49 (d, J = 5.4 Hz, 1H), 7.02 - 7.05 (m, 2H), 7.23 - 7.33 (m, 4H), 7.43 (s, 1H), 7.53 - 7.55 (m, 2H), 8.50 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 527 (M⁺+1)

Example 644: N-(1-Benzyl-4-piperidyl)-N'-{3-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea

[0753] 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (134 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 1-benzyl-4-piperidineamine (86 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (112 mg, yield 68%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.44 - 1.53 (m, 2H), 1.96 - 1.98 (m, 2H), 2.12 - 2.17 (m, 2H), 2.80 - 2.83 (m, 2H), 3.49 (s, 2H), 3.72 - 3.74 (m, 1H), 4.03 (s, 3H), 4.04 (s, 3H), 5.18 (d, J = 7.8 Hz, 1H), 6.29 (d, J = 5.4 Hz, 1H), 7.12 (d, J = 8.8 Hz, 1H), 7.23 - 7.32 (m, 5H), 7.39 - 7.40 (m, 2H), 7.60 (s, 1H), 7.64 (d, J = 2.4 Hz, 1H), 8.44 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 547 (M⁺+1)

Example 645: N-[2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]-N'-[2-(diethylamino)ethyl]urea

[0754] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diethyl-1,2-ethanediamine (52 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (64 mg, yield 45%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.16 (t, J = 7.3 Hz, 6H), 2.75 - 2.83 (m, 6H), 3.45 - 3.49 (m, 2H), 4.07 (s, 6H),

6.41 (brs, 1H), 7.14 - 7.17 (m, 1H), 7.28 - 7.32 (m, 2H), 7.51 (s, 1H), 8.20 (d, J = 9.0 Hz, 1H), 8.62 (s, 1H)
Mass spectrometry value (ESI-MS, m/z): 474 (M⁺+1)

Example 646: N-[2-(Diethylamino)ethyl]-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-nitrophenyl}urea

[0755] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-nitroaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (131 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diethyl-1,2-ethanediamine (51 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (65 mg, yield 46%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.16 - 1.20 (m, 6H), 2.77 - 2.86 (m, 6H), 3.48 - 3.52 (m, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 6.48 (d, J = 5.4 Hz, 1H), 7.44 - 7.50 (m, 3H), 8.01 (d, J = 2.9 Hz, 1H), 8.53 (d, J = 5.1 Hz, 1H), 8.70 (d, J = 9.5 Hz, 1H), 9.79 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 484 (M⁺+1)

Example 647: N-[2-(Diethylamino)ethyl]-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}urea

[0756] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-nitroaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (131 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diethyl-1,2-ethanediamine (51 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (107 mg, yield 76%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.10 (t, J = 7.1 Hz, 6H), 2.67 (q, J = 7.1 Hz, 4H), 2.72 (t, J = 5.9 Hz, 2H), 3.40 - 3.44 (m, 2H), 4.075 (s, 3H), 4.079 (s, 3H), 6.07 (brs, 1H), 7.34 (s, 1H), 7.52 (s, 1H), 7.54 (dd, J = 2.7, J = 9.3 Hz, 1H), 8.13 (d, J = 2.9 Hz, 1H), 8.61 (s, 1H), 8.78 (d, J = 9.3 Hz, 1H), 9.82 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 485 (M⁺+1)

Example 648: N-[2-(Diethylamino)ethyl]-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-methylphenyl}urea

[0757] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (142 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diethyl-1,2-ethanediamine (56 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (48 mg, yield 33%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.39 (t, J = 7.3 Hz, 6H), 2.12 (s, 3H), 3.12 - 3.20 (m, 6H), 3.67 - 3.68 (m, 2H), 4.046 (s, 3H), 4.052 (s, 3H), 6.27 (d, J = 5.4 Hz, 1H), 7.00 (d, J = 8.5 Hz, 1H), 7.28 (s, 1H), 7.36 - 7.44 (m, 3H), 7.60 (s, 1H), 8.42 (d, J = 5.4 Hz, 1H)

Example 649: N-[2-(Diethylamino)ethyl]-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-methylphenyl}urea

[0758] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (142 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diethyl-1,2-ethanediamine (56 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (49 mg, yield 34%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.32 - 1.36 (m, 6H), 2.35 (s, 3H), 2.99 - 3.14 (m, 6H), 3.62 - 3.66 (m, 2H), 4.04 (s, 3H), 4.05 (s, 3H), 6.49 (d, J = 5.4 Hz, 1H), 6.97 - 7.00 (m, 2H), 7.28 (s, 1H), 7.41 (s, 1H), 7.55 (s, 1H), 7.72 (d, J = 9.3 Hz, 1H), 8.47 (d, J = 5.1 Hz, 1H)

Example 650: N-{2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-[2-(diethylamino)ethyl]urea

[0759] 2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diethyl-1,2-ethanediamine (52 mg) was added

thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (32 mg, yield 22%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.26 (t, J = 7.1 Hz, 6H), 2.91 - 2.99 (m, 6H), 3.55 - 3.59 (m, 2H), 4.04 (s, 3H), 4.05 (s, 3H), 6.49 (d, J = 5.1 Hz, 1H), 7.07 - 7.10 (m, 2H), 7.21 (d, J = 2.7 Hz, 1H), 7.28 (s, 1H), 7.42 (s, 1H), 7.51 (s, 1H), 8.16 (d, J = 9.0 Hz, 1H), 8.50 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 473 (M⁺+1)

Example 651: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[2-(diethylamino)ethyl]urea

[0760] 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diethyl-1,2-ethanediamine (52 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (59 mg, yield 41%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.41 (brs, 6H), 3.18 - 3.19 (m, 6H), 3.64 - 3.73 (m, 2H), 4.05 (s, 6H), 6.31 (s, 1H), 7.12 (d, J = 8.3 Hz, 1H), 7.42 (s, 2H), 7.60 (s, 1H), 7.81 (s, 1H), 8.46 (s, 1H), 8.88 (brs, 1H)

Mass spectrometry value (ESI-MS, m/z): 473 (M⁺+1)

Example 652: N-[4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-nitrophenyl]-N'-(2-morpholinoethyl)urea

[0761] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-nitroaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (131 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-morpholino-1-ethanamine (57 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (30 mg, yield 21%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.60 - 2.73 (m, 4H), 3.46 - 3.50 (m, 2H), 3.79 - 3.84 (m, 4H), 4.08 (s, 6H), 7.34 (s, 1H), 7.52 - 7.56 (m, 2H), 8.13 (d, J = 2.7 Hz, 1H), 8.61 (s, 1H), 8.78 (d, J = 9.5 Hz, 1H), 9.81 (s, 1H)

Example 653: N-[4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-nitrophenyl]-N'-(2-tetrahydro-1H-1-pyrrolylethyl)urea

[0762] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-nitroaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (131 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-tetrahydro-1H-1-pyrrolyl-1-ethanamine (50 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (42 mg, yield 30%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.90 (s, 4H), 2.74 (s, 4H), 2.82 (t, J = 5.6 Hz, 2H), 3.50 (q, J = 5.4 Hz, 2H), 4.075 (s, 3H), 4.078 (s, 3H), 7.34 (s, 1H), 7.52 - 7.55 (m, 2H), 8.12 (d, J = 2.9 Hz, 1H), 8.61 (s, 1H), 8.78 (d, J = 9.3 Hz, 1H), 9.82 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 483 (M⁺+1)

Example 654: N-[2-(Diisopropylamino)ethyl]-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]urea

[0763] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (151 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diisopropyl-1,2-ethanediamine (74 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (52 mg, yield 33%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.06 (d, J = 6.3 Hz, 12H), 2.67 (t, J = 4.9 Hz, 2H), 3.07 - 3.11 (m, 2H), 3.24 - 3.31 (m, 2H), 4.05 (s, 6H), 6.45 (d, J = 5.4 Hz, 1H), 7.13 (d, J = 8.8 Hz, 2H), 7.42 - 7.44 (m, 3H), 7.56 (s, 1H), 8.47 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 467 (M⁺+1)

Example 655: N-[2-(Diisopropylamino)ethyl]-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]urea

[0764] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diisopropyl-1,2-ethanediamine (68 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (46 mg, yield 30%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.01 - 1.15 (m, 12H), 2.12 (s, 3H), 2.28 (s, 3H), 2.62 (brs, 2H), 3.00 (brs, 2H), 3.28 (brs, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 6.25 (s, 1H), 6.99 (d, J = 8.8 Hz, 1H), 7.43 (s, 1H), 7.61 (s, 1H), 8.43 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 495 (M⁺+1)

Example 656: N-[2-(Diisopropylamino)ethyl]-N'-[4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]urea

[0765] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (151 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diisopropyl-1,2-ethanediamine (74 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (58 mg, yield 37%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.12 - 1.15 (m, 12H), 2.74 (brs, 2H), 3.16 (brs, 2H), 3.34 (brs, 2H), 4.067 (s, 3H), 4.073 (s, 3H), 7.19 (d, J = 9.0 Hz, 1H), 7.32 (s, 1H), 7.46 (d, J = 9.0 Hz, 1H), 7.56 (s, 1H), 8.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 468 (M⁺+1)

Example 657: N-[2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]-N'-[2-(diisopropylamino)ethyl]urea

[0766] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (134 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diisopropyl-1,2-ethanediamine (65 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (64 mg, yield 43%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.45 - 1.48 (m, 12H), 3.19 - 3.22 (m, 2H), 3.60 - 3.65 (m, 2H), 3.73 - 3.74 (m, 2H), 4.07 (s, 6H), 7.12 - 7.15 (m, 2H), 7.51 (s, 1H), 7.70 (s, 1H), 7.97 (s, 1H), 8.16 (d, J = 9.0 Hz, 1H), 8.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 502 (M⁺+1)

Example 658: N-[2-(Diisopropylamino)ethyl]-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-nitrophenyl]urea

[0767] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-nitroaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (131 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diisopropyl-1,2-ethanediamine (63 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (103 mg, yield 70%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.33 - 1.37 (m, 12H), 3.04 - 3.07 (m, 2H), 3.45 - 3.51 (m, 2H), 3.61 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), 6.49 (d, J = 5.1 Hz, 1H), 7.42 - 7.45 (m, 2H), 7.50 (s, 1H), 8.00 (d, J = 2.9 Hz, 1H), 8.52 (d, J = 5.4 Hz, 1H), 8.58 - 8.62 (m, 1H), 9.76 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 512 (M⁺+1)

Example 659: N-[2-(Diisopropylamino)ethyl]-N'-[4-[(6,7-dimethoxy-4-quinazolinyloxy)-2-nitrophenyl]urea

[0768] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-nitroaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (131 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diisopropyl-1,2-ethanediamine (63 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (71 mg, yield 48%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.20 - 1.23 (m, 12H), 2.87 (s, 2H), 3.27 - 3.28 (m, 2H), 3.45 - 3.49 (m, 2H), 4.075 (s, 3H), 4.080 (s, 3H), 7.34 (s, 1H), 7.52 (s, 1H), 7.54 (d, J = 2.9 Hz, 1H), 8.12 (d, J = 2.7 Hz, 1H), 8.61 (s, 1H), 8.74 (d, J = 9.3 Hz, 1H), 9.84 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 513 (M⁺+1)

Example 660: N-[2-(Diisopropylamino)ethyl]-N'-[4-[(6,7-dimethoxy-4-quinazolinyloxy)-2-methoxyphenyl]urea

[0769] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-methoxyaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diisopropyl-1,2-ethanediamine (68 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (50 mg, yield 32%).

[0770] ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.07 (brs, 12H), 2.69 (brs, 2H), 3.10 (brs, 2H), 3.27 (brs, 2H), 3.84 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), 6.44 (d, J = 5.1 Hz, 1H), 7.72 (d, J = 2.4 Hz, 1H), 6.78 (dd, J = 2.7, 8.8 Hz, 1H), 7.42 (s, 1H), 7.56 (s, 1H), 8.05 (d, J = 9.0 Hz, 1H), 8.48 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 497 (M⁺+1)

Example 661: N-[4-[(6,7-Dimethoxy-4-quinolyloxy)phenyl]-N'-[2-(ethyl-3-methylanilino)ethyl]urea

[0771] 4-[(6,7-Dimethoxy-4-quinolyloxy)aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (151 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1-ethyl-N1-(3-methylphenyl)-1,2-ethanediamine (91 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (139 mg, yield 82%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.15 (t, J = 7.1 Hz, 3H), 2.30 (s, 3H), 3.39 (q, J = 7.1 Hz, 2H), 3.48 (s, 4H), 4.05 (s, 3H), 4.06 (s, 3H), 6.44 (d, J = 5.4 Hz, 1H), 6.56 (d, J = 7.1 Hz, 1H), 6.61 (s, 2H), 7.09 - 7.15 (m, 3H), 7.35 (d, J = 8.8 Hz, 2H), 7.46 (s, 1H), 7.55 (s, 1H), 8.46 (d, J = 5.4 Hz, 1H)

Example 662: N-[4-[(6,7-Dimethoxy-4-quinolyloxy)-2,5-dimethylphenyl]-N'-[2-(ethyl-3-methylanilino)ethyl]urea

[0772] 4-[(6,7-Dimethoxy-4-quinolyloxy)-2,5-dimethylaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1-ethyl-N1-(3-methylphenyl)-1,2-ethanediamine (84 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (137 mg, yield 84%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.13 (t, J = 7.1 Hz, 3H), 2.09 (s, 3H), 2.21 (s, 3H), 2.30 (s, 3H), 3.37 (q, J = 6.8 Hz, 2H), 3.46 (s, 4H), 4.06 (s, 6H), 4.84 (s, 1H), 5.92 (s, 1H), 6.27 (d, J = 5.1 Hz, 1H), 6.53 - 6.57 (m, 3H), 6.95 (s, 1H), 7.09 - 7.13 (m, 1H), 7.31 (s, 1H), 7.45 (s, 1H), 7.57 (s, 1H), 8.44 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 529 (M⁺+1)

Example 663: N-[4-[(6,7-Dimethoxy-4-quinolyloxy)-2,3-dimethylphenyl]-N'-[2-(ethyl-3-methylanilino)ethyl]urea

[0773] 4-[(6,7-Dimethoxy-4-quinolyloxy)-2,3-dimethylaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1-ethyl-N1-(3-methylphenyl)-1,2-ethanediamine (84 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (112 mg, yield 68%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.12 (t, J = 7.1 Hz, 3H), 2.10 (s, 3H), 2.24 (s, 3H), 2.30 (s, 3H), 3.35 (q, J = 6.8 Hz, 2H), 3.45 (s, 4H), 4.07 (s, 6H), 6.57 (s, 1H), 6.95 (d, J = 8.5 Hz, 1H), 7.60 (s, 1H), 8.43 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 529 (M⁺+1)

Example 664: N-[4-[(6,7-Dimethoxy-4-quinazolinyloxy)phenyl]-N'-[2-(ethyl-3-methylanilino)ethyl]urea

[0774] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine

(1 ml) to prepare a solution. A solution of triphosgene (151 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1-ethyl-N1-(3-methylphenyl)-1,2-ethanediamine (91 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (177 mg, yield 100%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.07 - 1.16 (m, 3H), 2.31 (s, 3H), 3.39 - 3.48 (m, 6H), 4.07 (s, 6H), 7.16 - 7.19 (m, 3H), 7.32 - 7.35 (m, 2H), 7.55 (s, 1H), 8.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

Example 665: N-[2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]-N'-[2-(ethyl-3-methylanilino)ethyl]urea

[0775] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (134 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1-ethyl-N1-(3-methylphenyl)-1,2-ethanediamine (80 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (146 mg, yield 91%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.09 - 1.17 (m, 3H), 2.31 (s, 3H), 3.41 - 3.50 (m, 6H), 4.07 (s, 6H), 6.60 (s, 1H), 7.31 - 7.33 (m, 2H), 7.52 (s, 1H), 8.18 (d, J = 9.0 Hz, 1H), 8.63 (s, 1H)

Example 666: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-nitrophenyl]-N'-[2-(ethyl-3-methylanilino)ethyl]urea

[0776] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-nitroaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (131 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1-ethyl-N1-(3-methylphenyl)-1,2-ethanediamine (78 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (101 mg, yield 64%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.17 (t, J = 7.1 Hz, 3H), 2.31 (s, 3H), 3.39 - 3.44 (q, J = 7.1 Hz, 2H), 3.52 (s, 4H), 4.05 (s, 3H), 4.07 (s, 3H), 6.49 (d, J = 5.4 Hz, 1H), 6.58 - 6.62 (m, 2H), 7.12 - 7.14 (m, 1H), 7.47 - 7.51 (m, 3H), 8.04 (d, J = 2.9 Hz, 1H), 8.53 (d, J = 5.4 Hz, 1H), 8.78 (d, J = 9.5 Hz, 1H), 9.68 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 546 (M⁺+1)

Example 667: N-[4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-nitrophenyl]-N'-[2-(ethyl-3-methylanilino)ethyl]urea

[0777] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-nitroaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (131 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1-ethyl-N1-(3-methylphenyl)-1,2-ethanediamine (78 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (110 mg, yield 69%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.07 - 1.19 (m, 3H), 2.30 - 2.31 (m, 3H), 3.36 - 3.42 (m, 2H), 3.52 (s, 4H), 4.078 (s, 3H), 4.083 (s, 3H), 6.57 - 6.61 (m, 4H), 7.35 (s, 1H), 7.52 - 7.57 (m, 2H), 8.14 (d, J = 2.9 Hz, 1H), 8.61 (s, 1H), 8.80 (d, J = 9.8 Hz, 1H), 9.74 (s, 1H)

Example 668: N-[4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-methoxyphenyl]-N'-[2-(ethyl-3-methylanilino)ethyl]urea

[0778] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-methoxyaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1-ethyl-N1-(3-methylphenyl)-1,2-ethanediamine (84 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (140 mg, yield 85%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.16 (t, J = 7.1 Hz, 3H), 2.31 (s, 3H), 3.40 (q, J = 7.1 Hz, 2H), 3.48 (s, 4H), 3.83 (s, 3H), 4.07 (s, 6H), 6.55 - 6.65 (m, 2H), 6.78 (d, J = 2.4 Hz, 1H), 6.83 (dd, J = 2.4, 8.8 Hz, 1H), 7.13 (s, 1H), 7.33 (s, 1H), 7.55 (s, 1H), 8.07 (d, J = 8.5 Hz, 1H), 8.64 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 532 (M⁺+1)

Example 669: N-[2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[2-(ethyl-3-methylanilino)ethyl]urea

[0779] 2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (134 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1-ethyl-N1-(3-methylphenyl)-1,2-ethanediamine (80 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (100 mg, yield 62%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.16 (t, J = 7.1 Hz, 3H), 2.30 (s, 3H), 3.40 (q, J = 7.1 Hz, 2H), 3.50 (s, 4H), 4.045 (s, 3H), 4.054 (s, 3H), 6.49 (d, J = 5.1 Hz, 1H), 6.56 (d, J = 7.6 Hz, 1H), 6.60 (s, 1H), 7.04 (d, J = 5.1 Hz, 1H), 7.09 - 7.13 (m, 1H), 7.21 (d, J = 2.7 Hz, 1H), 7.43 (d, J = 11.5 Hz, 2H), 7.51 (s, 1H), 8.19 - 8.22 (m, 1H), 8.50 (d, J = 5.1 Hz, 1H), 8.57 (d, J = 4.9 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 535 (M⁺+1)

Example 670: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methoxyphenyl]-N'-[2-(ethyl-3-methylanilino)ethyl]urea

[0780] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methoxyaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1-ethyl-N1-(3-methylphenyl)-1,2-ethanediamine (84 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (130 mg, yield 79%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.16 (t, J = 7.1 Hz, 3H), 2.30 (s, 3H), 3.40 (q, J = 7.1 Hz, 2H), 3.49 (s, 4H), 3.81 (s, 3H), 4.06 (s, 6H), 6.48 (d, J = 5.4 Hz, 1H), 6.55 (d, J = 7.3 Hz, 1H), 6.60 (s, 1H), 6.70 (d, J = 2.4 Hz, 1H), 6.79 (dd, J = 2.4, 8.8 Hz, 1H), 7.11 - 7.15 (m, 1H), 7.45 (s, 1H), 7.56 (s, 1H), 8.10 (d, J = 8.3 Hz, 1H), 8.48 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 531 (M⁺+1)

Example 671: N-[2-(Diisopropylamino)ethyl]-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]urea

[0781] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diisopropyl-1,2-ethanediamine (68 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (63 mg, yield 41%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.00 (brs, 12H), 2.13 (s, 3H), 2.27 (s, 3H), 2.63 (brs, 2H), 3.02 (brs, 2H), 3.27 (brs, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 6.29 (d, J = 5.1 Hz, 1H), 6.98 (s, 1H), 7.43 (s, 1H), 7.59 (s, 1H), 8.44 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 495 (M⁺+1)

Example 672: N-[2-(Diisopropylamino)ethyl]-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-methoxyphenyl]urea

[0782] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methoxyaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-diisopropyl-1,2-ethanediamine (68 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (80 mg, yield 52%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.02 - 1.15 (m, 12H), 3.03 (brs, 2H), 3.26 (brs, 2H), 3.48 - 3.50 (m, 2H), 3.86 (s, 3H), 4.07 (s, 3H), 6.79 - 6.84 (m, 3H), 7.32 (s, 1H), 7.55 (s, 1H), 8.07 (s, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 498 (M⁺+1)

Example 673: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2-piperidinoethyl)urea

[0783] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (151 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-piperidino-1-ethanamine (65 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using

chloroform/methanol to give the title compound (119 mg, yield 78%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.51 - 1.70 (m, 6H), 2.44 - 2.65 (m, 6H), 3.41 - 3.45 (m, 2H), 4.04 (s, 6H), 6.45 (d, J = 5.4 Hz, 1H), 7.11 (d, J = 8.8 Hz, 2H), 7.27 (s, 1H), 7.41 (s, 1H), 7.49 (d, J = 8.8 Hz, 2H), 7.56 (s, 1H), 8.46 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 451 (M⁺+1)

Example 674: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl}-N'-(2-piperidinoethyl)urea

[0784] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-piperidino-1-ethanamine (60 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (123 mg, yield 83%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.57 - 1.63 (m, 6H), 2.14 (s, 3H), 2.27 (s, 3H), 2.50 - 2.59 (m, 6H), 3.40 - 3.44 (m, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 5.80 (s, 1H), 6.31 (d, J = 5.1 Hz, 1H), 6.96 (s, 1H), 7.27 (s, 1H), 7.42 (s, 1H), 7.49 (s, 1H), 7.59 (s, 1H), 8.44 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 479 (M⁺+1)

Example 675: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}-N'-(2-piperidinoethyl)urea

[0785] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-piperidino-1-ethanamine (60 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (48 mg, yield 32%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.00 (brs, 6H), 2.09 (s, 3H), 2.30 (s, 3H), 3.08 - 3.18 (m, 6H), 3.70 - 3.74 (m, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 6.29 (d, J = 5.1 Hz, 1H), 6.94 (d, J = 8.8 Hz, 1H), 7.28 (s, 1H), 7.43 (s, 1H), 7.52 (d, J = 8.8 Hz, 1H), 7.62 (s, 1H), 8.42 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 479 (M⁺+1)

Example 676: N-{4-[(6,7-Dimethoxy-4-quinazolinyloxy)phenyl]-N'-(2-piperidinoethyl)urea

[0786] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (151 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-piperidino-1-ethanamine (65 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (84 mg, yield 55%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.03 (brs, 6H), 3.09 - 3.18 (m, 6H), 3.66 - 3.76 (m, 2H), 4.060 (s, 3H), 4.063 (s, 3H), 6.73 (brs, 1H), 7.13 (d, J = 8.8 Hz, 2H), 7.30 (s, 1H), 7.35 (brs, 1H), 7.54 (s, 1H), 7.59 (d, J = 8.8 Hz, 2H), 8.58 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 452 (M⁺+1)

Example 677: N-[2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]-N'-(2-piperidinoethyl)urea

[0787] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (134 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-piperidino-1-ethanamine (58 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (118 mg, yield 81%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.84 - 1.88 (m, 6H), 2.86 - 2.92 (m, 6H), 3.52 - 3.62 (m, 2H), 4.06 (s, 6H), 6.16 (brs, 1H), 6.98 (brs, 1H), 7.14 (dd, J = 2.7, 9.0 Hz, 1H), 7.30 (d, J = 2.7 Hz, 1H), 7.32 (s, 1H), 7.52 (s, 1H), 8.23 (d, J = 9.0 Hz, 1H), 8.61 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 486 (M⁺+1)

Example 678: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-nitrophenyl}-N'-(2-piperidinoethyl)urea

[0788] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-nitroaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (131 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-piperidino-1-ethanamine (56 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (58 mg, yield 40%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.69 - 1.82 (m, 6H), 2.59 - 2.81 (m, 6H), 3.49 - 3.50 (m, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 5.95 (brs, 1H), 6.48 (d, J = 5.4 Hz, 1H), 7.44 (s, 1H), 7.47 (d, J = 2.9 Hz, 1H), 7.50 (s, 1H), 8.01 (d, J = 2.9 Hz, 1H), 8.53 (d, J = 5.1 Hz, 1H), 8.73 (d, J = 9.3 Hz, 1H), 9.78 (s, 1H)

Example 679: N-{4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-nitrophenyl]-N'-(2-piperidinoethyl)urea

[0789] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-nitroaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (131 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-piperidino-1-ethanamine (56 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (79 mg, yield 55%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.49 - 1.66 (m, 6H), 2.48 (brs, 4H), 2.57 (t, J = 5.9 Hz, 2H), 3.43 - 3.45 (m, 2H), 4.077 (s, 3H), 4.082 (s, 3H), 5.82 (s, 1H), 7.34 (s, 1H), 7.52 (s, 1H), 7.54 (dd, J = 2.9, 9.5 Hz, 1H), 8.14 (d, J = 2.7 Hz, 1H), 8.61 (s, 1H), 8.81 (d, J = 9.5 Hz, 1H), 9.81 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 497 (M⁺+1)

Example 680: N-{4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-methoxyphenyl]-N'-(2-piperidinoethyl)urea

[0790] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)-2-methoxyaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-piperidino-1-ethanamine (60 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (80 mg, yield 54%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.96 (brs, 6H), 2.97 - 3.02 (m, 6H), 3.59 - 3.65 (m, 2H), 3.87 (s, 3H), 4.07 (s, 6H), 6.37 (brs, 1H), 6.77 (d, J = 2.4 Hz, 1H), 6.81 (dd, J = 2.4, 8.8 Hz, 1H), 7.32 (s, 1H), 7.37 (s, 1H), 7.55 (s, 1H), 8.18 (d, J = 8.8 Hz, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 482 (M⁺+1)

Example 681: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methoxyphenyl}-N'-(2-piperidinoethyl)urea

[0791] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methoxyaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 2-piperidino-1-ethanamine (60 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (100 mg, yield 67%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 1.97 - 1.98 (m, 6H), 3.00 - 3.09 (m, 6H), 3.60 - 3.68 (m, 2H), 3.85 (s, 3H), 4.050 (s, 3H), 4.054 (s, 3H), 6.42 (brs, 1H), 6.48 (d, J = 5.4 Hz, 1H), 6.70 (d, J = 2.4 Hz, 1H), 6.76 (dd, J = 2.4, 8.8 Hz, 1H), 7.42 (s, 1H), 7.48 (s, 1H), 7.57 (s, 1H), 8.14 (d, J = 8.8 Hz, 1H), 8.47 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 481 (M⁺+1)

Example 682: N-[2-(Dibutylamino)ethyl]-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}urea

[0792] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (151 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-dibutyl-1,2-ethanediamine (88 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column

using chloroform/methanol to give the title compound (72 mg, yield 43%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.96 (t, J = 7.6 Hz, 6H), 1.34 - 1.42 (m, 4H), 1.65 - 1.73 (m, 4H), 2.90 - 2.94 (m, 4H), 3.08 (brs, 2H), 3.59 - 3.60 (m, 2H), 4.04 (s, 6H), 6.44 (d, J = 5.4 Hz, 1H), 7.10 (d, J = 9.0 Hz, 2H), 7.41 (s, 1H), 7.52 (d, J = 9.0 Hz, 2H), 7.56 (s, 1H), 8.46 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 495 (M⁺+1)

Example 683: N-[2-(Dibutylamino)ethyl]-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]urea

[0793] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-dibutyl-1,2-ethanediamine (81 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (82 mg, yield 51%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.89 (t, J = 7.3 Hz, 6H), 1.21 - 1.28 (m, 4H), 1.35 - 1.41 (m, 4H), 2.14 (s, 3H), 2.27 (s, 3H), 2.46 (t, J = 7.6 Hz, 4H), 2.61 - 2.64 (m, 2H), 3.34 - 3.38 (m, 2H), 4.055 (s, 3H), 4.058 (s, 3H), 6.29 (d, J = 5.1 Hz, 1H), 6.97 (s, 1H), 7.40 (s, 1H), 7.43 (s, 1H), 7.59 (s, 1H), 8.45 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 523 (M⁺+1)

Example 684: N-[2-(Dibutylamino)ethyl]-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]urea

[0794] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-dibutyl-1,2-ethanediamine (81 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (80 mg, yield 49%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.86 - 0.93 (m, 6H), 1.12 - 1.47 (m, 8H), 2.13 (s, 3H), 2.29 (s, 3H), 2.40 - 2.49 (m, 4H), 2.57 - 2.62 (m, 2H), 3.24 - 3.36 (m, 2H), 4.055 (s, 3H), 4.063 (s, 3H), 6.26 (d, J = 5.1 Hz, 1H), 6.98 (d, J = 8.5 Hz, 1H), 7.30 (d, J = 8.5 Hz, 1H), 7.43 (s, 1H), 7.61 (s, 1H), 8.43 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 523 (M⁺+1)

Example 685: N-[2-(Dibutylamino)ethyl]-N'-[4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]urea

[0795] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (151 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-dibutyl-1,2-ethanediamine (88 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (110 mg, yield 65%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.92 (t, J = 7.3 Hz, 6H), 1.25 - 1.32 (m, 4H), 1.45 - 1.52 (m, 4H), 2.54 - 2.58 (m, 4H), 2.68 - 2.71 (m, 2H), 3.36 - 3.37 (m, 2H), 4.06 (s, 6H), 7.18 (d, J = 8.5 Hz, 2H), 7.32 (s, 1H), 7.47 (d, J = 8.5 Hz, 2H), 7.55 (s, 1H), 8.61 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 496 (M⁺+1)

Example 686: N-[2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]-N'-[2-(dibutylamino)ethyl]urea

[0796] 2-Chloro-4-[(6,7-dimethoxy-4-quinazolinyloxy)aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (134 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-dibutyl-1,2-ethanediamine (78 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (69 mg, yield 43%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.93 (t, J = 7.3 Hz, 6H), 1.28 - 1.33 (m, 4H), 1.40 - 1.46 (m, 4H), 2.47 (t, J = 7.6 Hz, 4H), 2.60 - 2.63 (m, 2H), 3.32 - 3.35 (m, 2H), 4.07 (s, 6H), 7.17 (dd, J = 2.7, 9.0 Hz, 1H), 7.32 (d, J = 2.7 Hz, 1H), 7.33 (s, 1H), 7.52 (s, 1H), 8.19 (d, J = 9.0 Hz, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 530 (M⁺+1)

Example 687: N-[2-(Dibutylamino)ethyl]-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}urea

[0797] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-nitroaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (131 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-dibutyl-1,2-ethanediamine (76 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (66 mg, yield 42%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.89 - 0.96 (m, 6H), 1.27 - 1.38 (m, 4H), 1.42 - 1.49 (m, 4H), 2.48 (t, J = 7.3 Hz, 4H), 2.62 - 2.65 (m, 2H), 3.35 - 3.37 (m, 2H), 4.076 (s, 3H), 4.080 (s, 3H), 7.34 (s, 1H), 7.52 - 7.56 (m, 2H), 8.14 (d, J = 2.9 Hz, 1H), 8.61 (s, 1H), 8.81 (d, J = 9.3 Hz, 1H), 9.81 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 541 (M⁺+1)

Example 688: N-[2-(Dibutylamino)ethyl]-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-methoxyphenyl}urea

[0798] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-methoxyaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-dibutyl-1,2-ethanediamine (81 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (79 mg, yield 49%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.90 - 0.95 (m, 6H), 1.29 - 1.36 (m, 4H), 1.44 - 1.51 (m, 4H), 2.53 (t, J = 7.6 Hz, 4H), 2.66 - 2.69 (m, 2H), 3.35 - 3.38 (m, 2H), 3.86 (s, 3H), 4.07 (s, 3H), 4.09 (s, 3H), 6.78 (d, J = 2.4 Hz, 1H), 6.83 (dd, J = 2.4, 8.8 Hz, 1H), 6.96 (brs, 1H), 7.32 (s, 1H), 7.55 (s, 1H), 8.10 (d, J = 8.8 Hz, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 526 (M⁺+1)

Example 689: N-[2-(Dibutylamino)ethyl]-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-methoxyphenyl}urea

[0799] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methoxyaniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (139 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, N1,N1-dibutyl-1,2-ethanediamine (81 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (56 mg, yield 34%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 0.90 - 0.95 (m, 6H), 1.28 - 1.37 (m, 9H), 1.46 - 1.54 (m, 4H), 2.56 - 2.60 (m, 4H), 2.72 - 2.74 (m, 2H), 3.35 - 3.43 (m, 2H), 3.84 (s, 3H), 4.05 (s, 6H), 6.48 (d, J = 5.1 Hz, 1H), 6.71 (d, J = 2.4 Hz, 1H), 6.78 (dd, J = 2.4, 8.8 Hz, 1H), 7.42 (s, 1H), 7.57 (s, 1H), 8.09 (d, J = 8.5 Hz, 1H), 8.48 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 525 (M⁺+1)

Example 690: N1-[4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl]-4-benzyl-1-piperazinecarboxamide

[0800] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (151 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 1-benzylpiperazine (90 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (93 mg, yield 55%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.51 (t, J = 4.9 Hz, 4H), 3.52 (t, J = 5.1 Hz, 4H), 3.56 (s, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 6.44 (s, 1H), 7.18 (d, J = 8.8 Hz, 2H), 7.26 - 7.35 (m, 5H), 7.47 (d, J = 9.0 Hz, 2H), 7.55 (s, 1H), 8.61 (s, 1H)

Example 691: N1-[4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl]-4-phenyl-1-piperazinecarboxamide

[0801] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (100 mg) was dissolved in chloroform (10 ml) and triethylamine (1 ml) to prepare a solution. A solution of triphosgene (151 mg) in chloroform was then added to the solution, and the mixture was stirred at room temperature for 10 min. Next, 1-phenylpiperazine (83 mg) was added thereto, and the mixture was further stirred at room temperature for one hr. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by concentration. The residue was purified on a column using chloroform/methanol to give the title compound (130 mg, yield 79%)

¹H-NMR (CDCl₃-d₁, 400 MHz) : δ 3.27 (t, J = 5.1 Hz, 4H), 3.69 (t, J = 5.1 Hz, 4H), 4.066 (s, 3H), 4.072 (s, 3H), 6.50 (s, 1H), 6.90 - 6.97 (m, 3H), 7.20 (d, J = 8.8 Hz, 2H), 7.28 - 7.32 (m, 2H), 7.49 (d, J = 8.8 Hz, 2H), 7.56 (s, 1H), 8.62 (s, 1H)

Example 692: N-[(5-Bromo-2-thienyl)carbonyl]-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-methylphenyl}thiourea

[0802] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 5-bromo-2-thiophenecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 5-bromo-2-thiophene isothiocyanate was prepared using the resultant 5-bromo-2-thiophenecarbonyl chloride as a starting compound according to the description of the literature. 5-Bromo-2-thiophenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 18 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (58 mg, yield 65%).

¹H-NMR (DMSO-d₆, 400 MHz) : δ 2.26 (s, 3H), 3.94 (s, 3H), 3.96 (s, 3H), 6.53 (d, J = 5.4 Hz, 1H), 7.11 - 7.16 (m, 1H), 7.21 - 7.24 (m, 1H), 7.37 - 7.45 (m, 2H), 7.49 - 7.54 (m, 1H), 7.82 - 7.85 (m, 1H), 8.51 (d, J = 5.1 Hz, 1H), 10.04 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 559 (M⁺+1)

Example 693: N-[(5-Bromo-2-thienyl)carbonyl]-N'-{3-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[0803] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 5-bromo-2-thiophenecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 5-bromo-2-thiophene isothiocyanate was prepared using the resultant 5-bromo-2-thiophenecarbonyl chloride as a starting compound according to the description of the literature. 5-Bromo-2-thiophenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 18 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (65 mg, yield 75%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 6.39 (d, J = 5.4 Hz, 1H), 7.39 - 7.43 (m, 2H), 7.45 - 7.55 (m, 2H), 7.77 - 7.81 (m, 1H), 7.88 (d, J = 4.1 Hz, 1H), 8.12 (d, J = 2.4 Hz, 1H), 8.49 (d, J = 5.1 Hz, 1H), 10.55 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 579 (M⁺+1)

Example 694: N-[(5-Chloro-2-thienyl)carbonyl]-N'-{4[(6,7-dimethoxy-4-quinolyl)oxy]-2-methylphenyl}thiourea

[0804] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 5-chloro-2-thiophenecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 5-chloro-2-thiophene isothiocyanate was prepared using the resultant 5-chloro-2-thiophenecarbonyl chloride as a starting compound according to the description of the literature. 5-Chloro-2-thiophenecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (43 mg, yield 52%).

¹H-NMR (DMSO-d₆, 400 MHz) : δ 2.26 (s, 3H), 3.93 (s, 3H), 3.95 (s, 3H), 6.52 (d, J = 5.1 Hz, 1H), 7.11 - 7.15 (m, 1H), 7.21 - 7.23 (m, 1H), 7.27 - 7.29 (m, 1H), 7.38 - 7.46 (m, 3H), 7.86 - 7.88 (m, 1H), 8.51 (d, J = 5.1 Hz, 1H), 10.05 - 10.08 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 514 (M⁺+1)

Example 695: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-[(5-chloro-2-thienyl)carbonyl]thiourea

[0805] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 5-chloro-2-thiophenecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 5-chloro-2-thiophene isothiocyanate was prepared using the resultant 5-chloro-2-thiophenecarbonyl chloride as a starting compound according to the description of the literature. 5-Chloro-2-thiophenecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (46 mg, yield 58%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 6.38 (d, J = 5.4 Hz, 1H), 7.31 (d, J = 4.1 Hz, 1H), 7.41 (s, 1H), 7.46 (s, 1H), 7.49 (s, 1H), 7.77 - 7.82 (m, 1H), 7.92 - 7.95 (m, 1H), 8.10 - 8.12 (m, 1H), 8.48 (d, J = 5.1 Hz, 1H), 10.57 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 535 (M⁺+1)

Example 696: N-{4-[(6,7-Dimethoxy-4-quinolyl)-oxy]-2-methylphenyl}-N'-[3-(methylthio)propanoyl]-thiourea

[0806] 3-(Methylthio)propanoyl isothiocyanate was prepared using commercially available 3-(methylthio)propanoyl chloride (80 mg) as a starting compound according to the description of the literature. 3-(Methylthio)propanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 19 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (27 mg, yield 35%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.10 (s, 3H), 2.24 (s, 3H), 2.74 - 2.84 (m, 4H), 3.93 (s, 3H), 3.95 (s, 3H), 6.55 (d, J = 5.4 Hz, 1H), 7.11 - 7.72 (m, 5H), 8.52 (d, J = 5.4 Hz, 1H), 11.57 - 11.60 (bs, 1H), 12.10 - 12.13 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 472 (M⁺+1)

Example 697: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[3-(methylthio)propanoyl]thiourea

[0807] 3-(Methylthio)propanoyl isothiocyanate was prepared using commercially available 3-(methylthio)propanoyl chloride (80 mg) as a starting compound according to the description of the literature. 3-(Methylthio)propanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (14 mg, yield 18%).

¹H-NMR (DMSO-d₆, 400 MHz) : δ 2.10 (s, 3H), 2.71 - 2.84 (m, 4H), 3.94 (s, 3H), 3.96 (s, 3H), 6.41 (d, J = 5.4 Hz, 1H), 7.31 - 7.72 (m, 5H), 8.50 (d, J = 5.1 Hz, 1H), 11.63 - 11.66 (bs, 1H), 12.49 - 12.52 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 492 (M⁺+1)

Example 698: N-{4-[(6,7-Dimethoxy-4-quinolyl)-oxy]-2-methylphenyl}-N'-[(2,5-dimethyl-3-furyl)carbonyl]thiourea

[0808] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2,5-dimethyl-3-furoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2,5-dimethyl-3-furancarboxyl isothiocyanate was prepared using the resultant 2,5-dimethyl-3-furancarboxyl chloride as a starting compound according to the description of the literature. 2,5-Dimethyl-3-furancarboxyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 15 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (41 mg, yield 52%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.26 (s, 3H), 2.28 (s, 3H), 2.55 (s, 3H), 3.93 (s, 3H), 3.96 (s, 3H), 6.56 (d, J = 5.1 Hz, 1H), 6.90 (s, 1H), 7.14 (dd, J = 2.7, 8.8 Hz, 1H), 7.23 (d, J = 2.7 Hz, 1H), 7.41 (s, 1H), 7.50 (s, 1H), 7.67 (t, J = 8.7 Hz, 1H), 8.53 (d, J = 5.1 Hz, 1H), 10.97 - 11.00 (bs, 1H), 12.33 - 12.36 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 492 (M⁺+1)

Example 699: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[(2,5-dimethyl-3-furyl)carbonyl]thiourea

[0809] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2,5-dimethyl-3-furoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2,5-dimethyl-3-furancarboxyl isothiocyanate was prepared using the resultant 2,5-dimethyl-3-furancarboxyl chloride as a starting compound according to the description of the literature. 2,5-Dimethyl-3-furancarboxyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 15 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (38 mg, yield 50%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.26 (s, 3H), 2.55 (s, 3H), 3.95 (s, 3H), 3.96 (s, 3H), 6.42 (d, J = 5.1 Hz, 1H), 6.89 (s, 1H), 7.43 (s, 1H), 7.49 (d, J = 8.8 Hz, 1H), 7.53 (s, 1H), 7.70 - 7.76 (m, 1H), 8.16 - 8.21 (m, 1H), 8.51 (d, J = 5.1 Hz, 1H), 11.03 - 11.05 (bs, 1H), 12.71 - 12.74 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 512 (M⁺+1)

Example 700: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylphenyl}-N'-[2-(2-thienyl)acetyl]thiourea

[0810] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-thienyl)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-thienyl)ethanoyl isothiocyanate was prepared using the resultant 2-(2-thienyl)ethanoyl chloride as a starting compound according to the description of the literature. 2-(2-Thienyl)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 15 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (18 mg, yield 23%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.23 (s, 3H), 3.81 (s, 1H), 3.95 (s, 3H), 3.98 (s, 3H), 4.08 (s, 1H), 6.63 (d, J = 5.4 Hz, 1H), 6.93 - 7.05 (m, 3H), 7.16 - 7.19 (m, 1H), 7.24 - 7.27 (m, 1H), 7.36 - 7.46 (m, 3H), 7.55 (s, 1H), 7.70 (d, J = 8.8 Hz, 1H), 8.60 (d, J = 5.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 494 (M⁺+1)

Example 701: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-[2-(2-thienyl)acetyl]thiourea

[0811] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-thienyl)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-thienyl)ethanoyl isothiocyanate was prepared using the resultant 2-(2-thienyl)ethanoyl chloride as a starting compound according to the description of the literature. 2-(2-Thienyl)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (15 mg, yield 20%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.81 (s, 1H), 4.00 (s, 3H), 4.02 (s, 3H), 4.08 (s, 1H), 6.68 (d, J = 5.6 Hz, 1H), 6.93 - 7.05 (m, 3H), 7.37 - 7.40 (m, 1H), 7.44 - 7.47 (m, 1H), 7.49 (s, 1H), 7.58 (d, J = 8.8 Hz, 1H), 7.67 (s, 1H), 7.74 - 7.79 (m, 1H), 8.16 - 8.20 (m, 1H), 8.71 (d, J = 5.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 514 (M⁺+1)

Example 702: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-[2-(2-methylphenyl)acetyl]thiourea

[0812] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-methylphenyl)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-methylphenyl)ethanoyl isothiocyanate was prepared using the resultant 2-(2-methylphenyl)ethanoyl chloride as a starting compound according to the description of the literature. 2-(2-Methylphenyl)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]-aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (45 mg, yield 57%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.30 (s, 3H), 3.89 (s, 2H), 3.96 (s, 3H), 3.98 (s, 3H), 6.51 (d, J = 5.6 Hz, 1H), 7.12 - 7.28 (m, 5H), 7.45 (s, 1H), 7.50 (d, J = 9.0 Hz, 1H), 7.58 (s, 1H), 7.70 - 7.75 (m, 1H), 8.58 (d, J = 5.6 Hz, 1H), 11.80 - 11.83 (bs, 1H), 12.44 - 12.48 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 522 (M⁺+1)

Example 703: N-{4-[(6,7-Dimethoxy-4-quinazolinyloxy]phenyl}-N'-[2-(2-methylphenyl)acetyl]thiourea

[0813] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-methylphenyl)acetic acid (80 mg), and the mixture was heated 100°C for one hr. The solvent was removed by distillation, and 2-(2-methylphenyl)ethanoyl isothiocyanate was prepared using the resultant 2-(2-methylphenyl)ethanoyl chloride as a starting compound according to the description of the literature. 2-(2-Methylphenyl)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (36 mg, yield 43%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.30 (s, 3H), 3.88 (s, 2H), 3.97 (s, 3H), 3.99 (s, 3H), 7.14 - 7.36 (m, 7H), 7.39 (s, 1H), 7.56 (s, 1H), 7.70 - 7.75 (m, 1H), 8.55 - 8.57 (bs, 1H), 11.70 - 11.73 (bs, 1H), 12.39 - 12.42 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 489 (M⁺+1)

Example 704: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2-cyclohexylacetyl)thiourea

[0814] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-cyclohexylacetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-cyclohexylethanoyl isothiocyanate was prepared using the resultant 2-cyclohexylethanoyl chloride as a starting compound according to the description of the literature. 2-Cyclohexylethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (36 mg, yield 46%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.88 - 1.30 (m, 5H), 1.58 - 1.80 (m, 6H), 2.07 (d, J = 6.6 Hz, 1H), 2.37 (d, J = 7.1 Hz, 1H), 3.94 (s, 3H), 3.96 (s, 3H), 6.41 (d, J = 5.4 Hz, 1H), 7.42 (s, 1H), 7.47 (d, J = 8.8 Hz, 1H), 7.53 (s, 1H), 7.67 - 7.72 (m, 1H), 8.14 - 8.18 (m, 1H), 8.51 (d, J = 5.1 Hz, 1H), 11.53 - 11.56 (bs, 1H), 12.59 - 12.63 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 514 (M⁺+1)

Example 705: N-(2-Cyclohexylacetyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}thiourea

[0815] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-cyclohexylacetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-cyclohexylethanoyl isothiocyanate was prepared using the resultant 2-cyclohexylethanoyl chloride as a starting compound according to the description of the literature. 2-Cyclohexylethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (30 mg, yield 44%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.93 - 1.30 (m, 5H), 1.58 - 1.81 (m, 6H), 2.37 (d, J = 7.1 Hz, 2H), 3.98 (s, 3H), 3.99 (s, 3H), 7.35 (d, J = 8.8 Hz, 2H), 7.40 (s, 1H), 7.57 (s, 1H), 7.73 (d, J = 9.0 Hz, 2H), 8.57 (s, 1H), 11.44 - 11.47 (bs, 1H), 12.58 (d, J = 4.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 481 (M⁺+1)

Example 706: N-Benzyl-N'-[3-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]thiourea

[0816] 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was added to toluene (2 ml) and ethanol (2 ml) to prepare a solution. Benzyl isothiocyanate (48 μl) was then added to the solution, and the mixture was stirred at 80°C for 6 hr. The reaction solution was concentrated, and ether and hexane were added to the residue. The resultant crystal was collected by filtration to give the title compound (46 mg, yield 65%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 4.77 (d, J = 5.1 Hz, 1H), 6.42 (d, J = 5.4 Hz, 1H), 7.25 - 7.55 (m, 9H), 7.95 - 8.01 (bs, 1H), 8.37 - 8.43 (bs, 1H), 8.51 (d, J = 5.1 Hz, 1H), 9.80 - 9.86 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 480 (M⁺+1)

Example 707: N-Benzyl-N'-{4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}thiourea

[0817] 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (50 mg) was dissolved in toluene (4 ml) and ethanol (6 ml) to prepare a solution. Benzyl isothiocyanate (81 μl) was added to the solution, and the mixture was stirred at 80°C for 6 hr. The reaction solution was concentrated, and ether and hexane were added to the residue. The resultant crystal was collected by filtration to give the title compound (74 mg, yield 98%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.97 (s, 3H), 3.99 (s, 3H), 4.73 - 4.79 (bs, 2H), 7.24 - 7.56 (m, 11H), 8.18 - 8.25 (bs, 1H), 8.55 (s, 1H), 9.63 - 9.67 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 447 (M⁺+1)

Example 708: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[2-(1-naphthyl)acetyl]thiourea

[0818] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(1-naphthyl)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(1-naphthyl)ethanoyl isothiocyanate was prepared using the resultant 2-(1-naphthyl)ethanoyl chloride as a starting compound according to the description of the literature. 2-(1-Naphthyl)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was

concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (67 mg, yield 78%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.94 (s, 3H), 3.96 (s, 3H), 4.36 (s, 2H), 6.45 (d, J = 5.4 Hz, 1H), 7.41 - 8.15 (m, 12H), 8.53 (d, J = 5.4 Hz, 1H), 11.97- 12.00 (bs, 1H), 12.39 - 12.42 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 558 (M⁺+1)

Example 709: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[2-(1-naphthyl)acetyl]thiourea

[0819] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(1-naphthyl)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(1-naphthyl)ethanoyl isothiocyanate was prepared using the resultant 2-(1-naphthyl)ethanoyl chloride as a starting compound according to the description of the literature. 2-(1-Naphthyl)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (24 mg, yield 27%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.92 (s, 3H), 3.95 (s, 3H), 4.08 (s, 2H), 6.68 (d, J = 8.8 Hz, 1H), 7.29 - 8.16 (m, 13H), 8.63 (s, 1H), 10.03 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 525 (M⁺+1)

Example 710: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-[2-(2-naphthyl)acetyl]thiourea

[0820] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-naphthyl)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-naphthyl)ethanoyl isothiocyanate was prepared using the resultant 2-(2-naphthyl)ethanoyl chloride as a starting compound according to the description of the literature. 2-(2-naphthyl)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (25 mg, yield 29%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.74 (s, 2H), 3.98 (s, 3H), 4.00 (s, 3H), 6.62 (d, J = 6.4 Hz, 1H), 7.40 - 7.93 (m, 11H), 8.15 - 8.20 (m, 1H), 8.66 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 558 (M⁺+1)

Example 711: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[2-(2-naphthyl)acetyl]thiourea

[0821] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-naphthyl)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-naphthyl)ethanoyl isothiocyanate was prepared using the resultant 2-(2-naphthyl)ethanoyl chloride as a starting compound according to the description of the literature. 2-(2-Naphthyl)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (33 mg, yield 38%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.74 (s, 2H), 3.91 (s, 3H), 3.92 (s, 3H), 6.68 (d, J = 8.8 Hz, 1H), 7.29 - 7.52 (m, 6H), 7.77 - 7.90 (m, 6H), 8.31 (s, 1H), 8.64 - 8.68 (bs, 1H), 9.96 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 525 (M⁺+1)

Example 712: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-[3-(3,4-dimethoxyphenyl)propanoyl]thiourea

[0822] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-(3,4-dimethoxyphenyl)propanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-(3,4-dimethoxyphenyl)propanoyl isothiocyanate was prepared using the resultant 3-(3,4-dimethoxyphenyl)propanoyl chloride as a starting compound according to the description of the literature. 3-(3,4-Dimethoxyphenyl)propanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (32 mg, yield 36%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.94 (t, J = 7.3 Hz, 2H), 2.72 - 2.89 (m, 2H), 3.69 - 3.76 (m, 6H), 3.99 (d, J = 5.6 Hz, 3H), 6.57 (d, J = 5.6 Hz, 1H), 6.70 - 6.89 (m, 3H), 7.47 (s, 1H), 7.54 (d, J = 8.8 Hz, 1H), 7.62 (s, 1H), 7.70 - 7.76 (m, 1H), 8.16 - 8.20 (m, 1H), 8.63 (d, J = 5.6 Hz, 1H), 11.63 - 11.64 (bs, 1H), 12.55 - 12.58 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 582 (M⁺+1)

Example 713: N-[3-(3,4-Dimethoxyphenyl)propanoyl]-N'-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]thiourea

[0823] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-(3,4-dimethoxyphenyl) propanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-(3,4-dimethoxyphenyl)propanoyl isothiocyanate was prepared using the resultant 3-(3,4-dimethoxyphenyl)propanoyl chloride as a starting compound according to the description of the literature. 3-(3,4-Dimethoxyphenyl)propanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy] aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (37 mg, yield 40%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.94 (t, J = 7.3 Hz, 2H), 2.59 - 2.65 (m, 1H), 2.84 - 2.89 (m, 1H), 3.71 (s, 3H), 3.73 (s, 3H), 3.98 (d, J = 5.9 Hz, 3H), 6.68 - 6.88 (m, 4H), 7.23 (d, J = 8.5 Hz, 2H), 7.38 (s, 1H), 7.55 (s, 1H), 7.67 (d, J = 8.8 Hz, 2H), 8.53 (s, 1H), 10.00 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 549 (M⁺+1)

Example 714: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[2-(2-chlorophenoxy)acetyl]thiourea

[0824] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-chlorophenoxy)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-chlorophenoxy)ethanoyl isothiocyanate was prepared using the resultant 2-(2-chlorophenoxy)ethanoyl chloride as a starting compound according to the description of the literature. 2-(2-Chlorophenoxy)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (29 mg, yield 37%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.95 (s, 3H), 3.95 (s, 3H), 4.88 (s, 2H), 6.35 (d, J = 5.1 Hz, 1H), 6.95 - 7.13 (m, 3H), 7.26 - 7.67 (m, 6H), 8.05 - 8.07 (bs, 1H), 8.30 - 8.32 (bs, 1H), 8.47 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 523 (M⁺+1)

Example 715: N-[2-(2-Chlorophenoxy)acetyl]-N'-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]thiourea

[0825] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-chlorophenoxy)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-chlorophenoxy)ethanoyl isothiocyanate was prepared using the resultant 2-(2-chlorophenoxy)ethanoyl chloride as a starting compound according to the description of the literature. 2-(2-Chlorophenoxy)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (21 mg, yield 21%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 4.55 (s, 6H), 4.76 (s, 2H), 6.71 (d, J = 8.5 Hz, 1H), 6.95 - 7.47 (m, 10H), 9.24 (s, 1H), 9.84 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 525 (M⁺+1)

Example 716: N-[4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl]-N'-(4-ethoxybenzoyl)thiourea

[0826] 4-Ethoxy-1-benzenecarbonyl isothiocyanate was prepared using 4-ethoxy-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 4-Ethoxy-1-benzenecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (72 mg, yield 89%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.37 (t, J = 7.1 Hz, 3H), 3.99 (s, 3H), 4.00 (s, 3H), 4.15 (q, J = 7.1 Hz, 2H), 7.06 (d, J = 8.8 Hz, 2H), 7.35 - 7.41 (m, 3H), 7.58 (s, 1H), 7.75 - 7.82 (m, 2H), 8.03 (d, J = 8.8 Hz, 2H), 8.58 (s, 1H),

11.40 (d, J = 2.9 Hz, 1H), 12.74 - 12.75 (bs, 1H)
Mass spectrometry value (ESI-MS, m/z): 505 (M⁺+1)

Example 717: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]-N'-[(2,5-dimethyl-3-furyl)carbonyl]thiourea

[0827] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2,5-dimethyl-3-furoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2,5-dimethyl-3-furancarbonyl isothiocyanate was prepared using the resultant 2,5-dimethyl-3-furancarbonyl chloride as a starting compound according to the description of the literature. 2,5-Dimethyl-3-furancarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethyl-aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (69 mg, yield 96%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.11 (s, 3H), 2.23 (s, 3H), 2.26 (s, 3H), 2.55 (s, 3H), 3.95 (s, 6H), 6.35 (d, J = 5.4 Hz, 1H), 6.91 (s, 1H), 7.16 (s, 1H), 7.41 (s, 1H), 7.55 - 7.61 (m, 2H), 8.49 (d, J = 5.1 Hz, 1H), 10.98 - 11.10 (bs, 1H), 11.31 - 11.34 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 506 (M⁺+1)

Example 718: N-[4-[(6,7-Dimethoxy-4-quinazolinyloxy)phenyl]-N'-[(2,5-dimethyl-3-furyl)carbonyl]thiourea

[0828] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2,5-dimethyl-3-furoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2,5-dimethyl-3-furancarbonyl isothiocyanate was prepared using the resultant 2,5-dimethyl-3-furancarbonyl chloride as a starting compound according to the description of the literature. 2,5-Dimethyl-3-furancarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (77 mg, yield 95%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.26 (s, 3H), 2.55 (s, 3H), 3.98 (s, 3H), 4.00 (s, 3H), 6.89 (s, 1H), 7.34 - 7.41 (m, 3H), 7.58 (s, 1H), 7.73 - 7.81 (m, 2H), 8.58 (s, 1H), 10.93 (d, J = 3.9 Hz, 1H), 12.67 - 12.70 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 479 (M⁺+1)

Example 719: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-pentanoylthiourea

[0829] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available pentanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and pentanoyl isothiocyanate was prepared using the resultant pentanoyl chloride as a starting compound according to the description of the literature. Pentanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (29 mg, yield 41%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.90 (t, J = 7.6 Hz, 3H), 1.28 - 1.39 (m, 2H), 1.52 - 1.63 (m, 2H), 3.95 (s, 3H), 3.97 (s, 3H), 6.45 (d, J = 5.1 Hz, 1H), 7.43 (s, 1H), 7.49 (d, J = 8.8 Hz, 1H), 7.55 (s, 1H), 7.67 - 7.73 (m, 1H), 8.14 - 8.18 (m, 1H), 8.53 (d, J = 5.4 Hz, 1H), 11.57 (d, J = 2.7 Hz, 1H), 12.58 (d, J = 4.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 474 (M⁺+1)

Example 720: N-[4-[(6,7-Dimethoxy-4-quinazolinyloxy)phenyl]-N'-pentanoylthiourea

[0830] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available pentanoic acid (80 mg) at 100°C for one hr. The solvent was removed by distillation, and pentanoyl isothiocyanate was prepared using the resultant pentanoyl chloride as a starting compound according to the description of the literature. Pentanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (17 mg, yield 23%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.86 (t, J = 7.3 Hz, 3H), 1.23 - 1.40 (m, 2H), 1.50 - 1.64 (m, 2H), 3.12 - 3.19 (m, 2H), 3.97 (s, 3H), 3.99 (s, 3H), 7.21 - 7.25 (m, 2H), 7.38 (s, 1H), 7.55 (s, 1H), 7.66 - 7.70 (m, 2H), 8.53 (s, 1H),

9.97 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 441 (M⁺+1)

Example 721: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-[3-(4-methylphenyl)propanoyl]thiourea

[0831] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-(4-methylphenyl)propanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-(4-methylphenyl)propanoyl isothiocyanate was prepared using the resultant 3-(4-methylphenyl)propanoyl chloride as a starting compound according to the description of the literature. 3-(4-Methylphenyl)propanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (90 mg, yield 99%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.25 (s, 3H), 2.47 (s, 2H), 2.76 (t, J = 7.6 Hz, 2H), 3.93 (s, 3H), 3.95 (s, 3H), 6.54 (d, J = 5.1 Hz, 1H), 7.04 - 7.16 (m, 4H), 7.30 (d, J = 8.8 Hz, 2H), 7.41 (s, 1H), 7.50 (s, 1H), 7.73 - 7.79 (m, 2H), 8.51 (d, J = 5.1 Hz, 1H), 11.51 - 11.54 (bs, 1H), 12.04 - 12.10 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

Example 722: N-[4-[(6,7-Dimethoxy-4-quinazolinyloxy]phenyl]-N'-[3-(4-methylphenyl)propanoyl]thiourea

[0832] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-(4-methylphenyl)propanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-(4-methylphenyl)propanoyl isothiocyanate was prepared using the resultant 3-(4-methylphenyl)propanoyl chloride as a starting compound according to the description of the literature. 3-(4-Methylphenyl)propanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (54 mg, yield 63%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.25 (s, 3H), 2.47 (s, 2H), 2.62 (t, J = 7.3 Hz, 2H), 3.97 (s, 3H), 3.99 (s, 3H), 6.67 (d, J = 9.0 Hz, 1H), 7.04 - 7.39 (m, 7H), 7.55 (s, 3H), 7.64 - 7.68 (m, 2H), 8.53 (s, 1H), 10.00 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 503 (M⁺+1)

Example 723: N-[2-(2-Chlorophenyl)acetyl]-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]thiourea

[0833] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-chlorophenyl)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-chlorophenyl)ethanoyl isothiocyanate was prepared using the resultant 2-(2-chlorophenyl)ethanoyl chloride as a starting compound according to the description of the literature. 2-(2-Chlorophenyl)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (77 mg, yield 89%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.92 (s, 3H), 3.95 (s, 3H), 4.04 (s, 2H), 6.54 (d, J = 5.1 Hz, 1H), 7.27 - 7.50 (m, 7H), 7.74 - 7.79 (m, 2H), 8.31 (s, 1H), 8.51 (d, J = 5.1 Hz, 1H), 11.80 - 11.83 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 508 (M⁺+1)

Example 724: N-[2-(2-Chlorophenyl)acetyl]-N'-[4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl]thiourea

[0834] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-chlorophenyl)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-chlorophenyl)ethanoyl isothiocyanate was prepared using the resultant 2-(2-chlorophenyl)ethanoyl chloride as a starting compound according to the description of the literature. 2-(2-Chlorophenyl)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (43 mg, yield 49%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.86 (s, 2H), 3.97 (s, 3H), 3.99 (s, 3H), 7.22 - 7.48 (m, 8H), 7.56 (s, 1H), 7.66 - 7.71 (m, 2H), 8.53 (s, 1H), 10.33 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 509 (M⁺+1)

Example 725: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(4-phenylbutanoyl)thiourea

[0835] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-phenylbutanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-phenylbutanoyl isothiocyanate was prepared using the resultant 4-phenylbutanoyl chloride as a starting compound according to the description of the literature. 4-Phenylbutanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (50 mg, yield 59%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.07 - 1.12 (m, 4H), 2.72 - 2.88 (m, 2H), 3.93 (s, 3H), 3.96 (s, 3H), 6.55 (d, J = 5.4 Hz, 1H), 7.19 - 7.35 (m, 7H), 7.41 (s, 1H), 7.51 (s, 1H), 7.72 - 7.78 (m, 2H), 8.52 (d, J = 5.1 Hz, 1H), 11.50 - 11.53 (bs, 1H), 12.48 (d, J = 4.9 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

Example 726: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(4-phenylbutanoyl)thiourea

[0836] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-phenylbutanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-phenylbutanoyl isothiocyanate was prepared using the resultant 4-phenylbutanoyl chloride as a starting compound according to the description of the literature. 4-Phenylbutanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (56 mg, yield 70%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.23 - 1.28 (m, 4H), 2.72 - 2.88 (m, 2H), 3.94 (s, 3H), 3.96 (s, 3H), 6.42 (d, J = 5.4 Hz, 1H), 7.18 - 7.35 (m, 5H), 7.43 (s, 1H), 7.47 (d, J = 8.8 Hz, 1H), 7.53 (s, 1H), 7.64 - 7.70 (m, 1H), 8.11 - 8.15 (m, 1H), 8.51 (d, J = 8.4 Hz, 1H), 11.58 - 11.61 (bs, 1H), 12.50 (d, J = 4.9 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 536 (M⁺+1)

Example 727: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(5-phenylpentanoyl)thiourea

[0837] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 5-phenylpentanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-phenylpentanoyl isothiocyanate was prepared using the resultant 4-phenylpentanoyl chloride as a starting compound according to the description of the literature. 4-Phenylpentanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (41 mg, yield 47%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.56 - 1.64 (m, 4H), 2.57 - 2.63 (m, 2H), 3.94 (s, 3H), 3.96 (s, 3H), 6.58 (d, J = 5.4 Hz, 1H), 7.15 - 7.34 (m, 7H), 7.42 (s, 1H), 7.53 (s, 1H), 7.75 - 7.81 (m, 2H), 8.55 (d, J = 5.4 Hz, 1H), 11.48 (d, J = 2.9 Hz, 1H), 12.53 (d, J = 4.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 516 (M⁺+1)

Example 728: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(5-phenylpentanoyl)thiourea

[0838] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 5-phenylpentanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-phenylpentanoyl isothiocyanate was prepared using the resultant 4-phenylpentanoyl chloride as a starting compound according to the description of the literature. 4-Phenylpentanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (47 mg, yield 57%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.56 - 1.64 (m, 4H), 2.56 - 2.63 (m, 2H), 3.95 (s, 3H), 3.96 (s, 3H), 6.44 (d, J

= 5.4 Hz, 1H), 7.15 - 7.32 (m, 5H), 7.43 (s, 1H), 7.48 (d, J = 8.8 Hz, 1H), 7.54 (s, 1H), 7.67 - 7.72 (m, 1H), 8.13 - 8.18 (m, 1H), 8.53 (d, J = 5.4 Hz, 1H), 11.55 - 11.59 (bs, 1H), 12.55 (d, J = 4.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 550 (M⁺+1)

5 Example 729: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-[2-(2-fluorophenyl)acetyl]thiourea

[0839] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-fluorophenyl)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-fluorophenyl)ethanoyl isothiocyanate was prepared using the resultant 2-(2-fluorophenyl)ethanoyl chloride as a starting compound according to the description of the literature. 2-(2-Fluorophenyl)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (55 mg, yield 66%).

15 ¹H-NMR (DMSO-d₆, 400 MHz): δ 3.76 (s, 2H), 3.93 (s, 3H), 3.95 (s, 3H), 6.46 (d, J = 5.4 Hz, 1H), 7.10 - 7.52 (m, 8H), 7.71 - 7.76 (m, 2H), 8.31 (s, 1H), 8.47 (d, J = 5.1 Hz, 1H), 10.36 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

20 Example 730: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[2-(2-fluorophenyl)acetyl]thiourea

[0840] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-fluorophenyl)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-fluorophenyl)ethanoyl isothiocyanate was prepared using the resultant 2-(2-fluorophenyl)ethanoyl chloride as a starting compound according to the description of the literature. 2-(2-Fluorophenyl)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (51 mg, yield 65%).

25 ¹H-NMR (DMSO-d₆, 400 MHz) : δ 3.78 (s, 2H), 3.96 (s, 3H), 3.97 (s, 3H), 6.44 (d, J = 5.6 Hz, 1H), 7.10 - 7.64 (m, 8H), 8.06 (d, J = 2.2 Hz, 1H), 8.31 (s, 1H), 8.53 (d, J = 5.6 Hz, 1H), 10.56 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 526 (M⁺+1)

30 Example 731: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-[3-(2-methylphenyl)propanoyl]thiourea

[0841] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-(2-methylphenyl)propanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-(2-methylphenyl)propanoyl isothiocyanate was prepared using the resultant 3-(2-methylphenyl)propanoyl chloride as a starting compound according to the description of the literature. 3-(2-Methylphenyl)propanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (14 mg, yield 16%).

35 ¹H-NMR (DMSO-d₆, 400 MHz): δ 2.31 (s, 3H), 2.73 - 2.93 (m, 4H), 3.94 (s, 3H), 3.96 (s, 3H), 6.57 (d, J = 5.1 Hz, 1H), 7.08 - 7.19 (m, 4H), 7.32 (d, J = 8.8 Hz, 2H), 7.42 (s, 1H), 7.52 (s, 1H), 7.74 - 7.81 (m, 2H), 8.53 (d, J = 5.4 Hz, 1H), 11.54 - 11.57 (bs, 1H), 12.53 (d, J = 2.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

40 Example 732: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[3-(2-methylphenyl)propanoyl]thiourea

[0842] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-(2-methylphenyl)propanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-(2-methylphenyl)propanoyl isothiocyanate was prepared using the resultant 3-(2-methylphenyl)propanoyl chloride as a starting compound according to the description of the literature. 3-(2-Methylphenyl)propanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (45 mg, yield 56%).

50 ¹H-NMR (DMSO-d₆, 400 MHz): δ 2.31 (s, 3H), 2.74 - 2.92 (m, 4H), 3.97 (s, 3H), 3.98 (s, 3H), 6.51 (d, J = 5.6 Hz,

1H), 7.08 - 7.20 (m, 4H), 7.45 (s, 1H), 7.52 (d, J = 8.8 Hz, 1H), 7.58 (s, 1H), 7.69 - 7.75 (m, 1H), 8.15 - 8.19 (m, 1H), 8.58 (d, J = 5.4 Hz, 1H), 11.65 (d, J = 2.4 Hz, 1H), 12.56 (d, J = 4.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 536 (M⁺+1)

5 Example 733: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-[2-(2-methoxyphenyl)acetyl]thiourea

[0843] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-methoxyphenyl)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-methoxyphenyl)ethanoyl isothiocyanate was prepared using the resultant 2-(2-methoxyphenyl)ethanoyl chloride as a starting compound according to the description of the literature. 2-(2-Methoxyphenyl)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (25 mg, yield 30%).

15 ¹H-NMR (DMSO-d₆, 400 MHz): δ 3.79 (s, 3H), 3.82 (s, 2H), 3.96 (s, 3H), 3.99 (s, 3H), 6.66 (d, J = 5.9 Hz, 1H), 6.85 - 7.03 (m, 2H), 7.21 - 7.37 (m, 4H), 7.44 (s, 1H), 7.58 (s, 1H), 7.78 - 7.84 (m, 2H), 8.62 (d, J = 5.9 Hz, 1H), 11.64 - 11.66 (bs, 1H), 12.47 (d, J = 4.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 504 (M⁺+1)

20 Example 734: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[2-(2-methoxyphenyl)acetyl]thiourea

[0844] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-methoxyphenyl)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-methoxyphenyl)ethanoyl isothiocyanate was prepared using the resultant 2-(2-methoxyphenyl)ethanoyl chloride as a starting compound according to the description of the literature. 2-(2-Methoxyphenyl)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (45 mg, yield 55%).

30 ¹H-NMR (DMSO-d₆, 400 MHz): δ 3.79 (s, 3H), 3.82 (s, 2H), 3.99 (s, 3H), 4.01 (s, 3H), 6.66 (d, J = 5.9 Hz, 1H), 6.85 - 7.03 (m, 2H), 7.22 - 7.32 (m, 2H), 7.49 (s, 1H), 7.56 (d, J = 9.0 Hz, 1H), 7.66 (s, 1H), 7.74 - 7.80 (m, 1H), 8.20 - 8.24 (m, 1H), 8.69 (d, J = 5.9 Hz, 1H), 11.75 (d, J = 2.4 Hz, 1H), 12.52 (d, J = 4.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 538 (M⁺+1)

35 Example 735: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-[2-(2-nitrophenyl)acetyl]thiourea

[0845] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-nitrophenyl)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-nitrophenyl)ethanoyl isothiocyanate was prepared using the resultant 2-(2-nitrophenyl)ethanoyl chloride as a starting compound according to the description of the literature. 2-(2-Nitrophenyl)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/methanol for development to give the title compound (7 mg, yield 8%).

45 ¹H-NMR (DMSO-d₆, 400 MHz): δ 4.00 (s, 3H), 4.00 (s, 3H), 4.30 (s, 2H), 6.71 (d, J = 5.9 Hz, 1H), 7.33 - 7.84 (m, 8H), 8.08 (d, J = 7.8 Hz, 1H), 8.67 (d, J = 5.9 Hz, 1H), 11.84 - 11.88 (bs, 1H), 12.25 - 12.28 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 519 (M⁺+1)

50 Example 736: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[2-(2-nitrophenyl)acetyl]thiourea

[0846] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-nitrophenyl)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-nitrophenyl)ethanoyl isothiocyanate was prepared using the resultant 2-(2-nitrophenyl)ethanoyl chloride as a starting compound according to the description of the literature. 2-(2-Nitrophenyl)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/methanol for development to give the title compound (8 mg, yield 10%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.94 (s, 3H), 3.96 (s, 3H), 4.30 (s, 2H), 6.41 (d, J = 5.1 Hz, 1H), 7.40 - 7.80 (m, 7H), 8.10 - 8.17 (m, 2H), 8.50 (d, J = 5.1 Hz, 1H), 11.91 - 11.94 (bs, 1H), 12.26 (d, J = 4.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 553 (M⁺+1)

5 Example 737: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2-phenoxyacetyl)thiourea

[0847] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-phenoxyacetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-phenoxyethanoyl isothiocyanate was prepared using the resultant 2-phenoxyethanoyl chloride as a starting compound according to the description of the literature. 2-Phenoxyethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (40 mg, yield 48%).

15 ¹H-NMR (DMSO-d₆, 400 MHz): δ 3.94 (s, 3H), 3.96 (s, 3H), 4.73 (s, 2H), 6.49 (d, J = 5.1 Hz, 1H), 6.88 - 7.05 (m, 3H), 7.24 - 7.36 (m, 4H), 7.40 (s, 1H), 7.53 (s, 1H), 7.80 (d, J = 9.0 Hz, 2H), 8.50 (d, J = 5.4 Hz, 1H), 10.25 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 490 (M⁺+1)

20 Example 738: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2-phenoxyacetyl)thiourea

[0848] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-phenoxyacetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-phenoxyethanoyl isothiocyanate was prepared using the resultant 2-phenoxyethanoyl chloride as a starting compound according to the description of the literature. 2-Phenoxyethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (50 mg, yield 64%).

30 ¹H-NMR (DMSO-d₆, 400 MHz): δ 3.99 (s, 3H), 4.00 (s, 3H), 4.76 (s, 2H), 6.57 (d, J = 5.6 Hz, 1H), 6.88 - 7.05 (m, 3H), 7.26 - 7.37 (m, 3H), 7.46 (s, 1H), 7.51 (d, J = 9.0 Hz, 1H), 7.63 (s, 1H), 7.73 - 7.78 (m, 1H), 8.12 (d, J = 2.2 Hz, 1H), 8.61 (d, J = 5.9 Hz, 1H), 10.44 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 524 (M⁺+1)

35 Example 739: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-[2-(2-methylphenoxy)acetyl]thiourea

[0849] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-methylphenoxy)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-methylphenoxy)ethanoyl isothiocyanate was prepared using the resultant 2-(2-methylphenoxy)ethanoyl chloride as a starting compound according to the description of the literature. 2-(2-Methylphenoxy)ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (25 mg, yield 29%).

45 ¹H-NMR (DMSO-d₆, 400 MHz): δ 2.27 (s, 3H), 3.94 (s, 3H), 3.95 (s, 3H), 4.74 (s, 2H), 6.46 (d, J = 5.1 Hz, 1H), 6.78 - 6.92 (m, 3H), 7.09 - 7.28 (m, 4H), 7.40 (s, 1H), 7.51 (s, 1H), 7.78 (d, J = 8.8 Hz, 2H), 8.47 (d, J = 5.1 Hz, 1H), 10.20 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 504 (M⁺+1)

50 Example 740: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[2-(2-methylphenoxy)acetyl]thiourea

[0850] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-methylphenoxy)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-methylphenoxy)ethanoyl isothiocyanate was prepared using the resultant 2-(2-methylphenoxy)ethanoyl chloride as a starting compound according to the description of the literature. 2-Phenoxyethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (26 mg, yield 32%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.27 (s, 3H), 3.96 (s, 3H), 3.96 (s, 3H), 4.77 (s, 2H), 6.42 (d, J = 5.4 Hz, 1H), 6.78 - 7.71 (m, 9H), 8.09 (d, J = 2.4 Hz, 1H), 8.51 (d, J = 5.4 Hz, 1H), 10.39 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 538 (M⁺+1)

5 Example 741: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-phenoxybutanoyl)thiourea

[0851] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-phenoxybutanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-phenoxybutanoyl isothiocyanate was prepared using the resultant 2-phenoxybutanoyl chloride as a starting compound according to the description of the literature. 2-Phenoxybutanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (35 mg, yield 40%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.05 (t, J = 7.3 Hz, 3H), 1.87 - 2.01 (m, 2H), 3.92 (s, 3H), 3.95 (s, 3H), 4.95 - 5.00 (m, 1H), 6.54 (d, J = 5.4 Hz, 1H), 6.88 - 7.02 (m, 3H), 7.25 - 7.37 (m, 4H), 7.41 (s, 1H), 7.49 (s, 1H), 7.73 - 7.80 (m, 2H), 8.52 (d, J = 5.4 Hz, 1H), 11.73 - 11.76 (bs, 1H), 12.16 (d, J = 4.9 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 518 (M⁺+1)

20 Example 742: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-phenoxybutanoyl)thiourea

[0852] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-phenoxybutanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-phenoxybutanoyl isothiocyanate was prepared using the resultant 2-phenoxybutanoyl chloride as a starting compound according to the description of the literature. 2-Phenoxybutanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (25 mg, yield 27%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.06 (t, J = 7.6 Hz, 3H), 1.86 - 2.02 (m, 2H), 3.94 (s, 3H), 3.96 (s, 3H), 4.95 - 5.01 (m, 1H), 6.40 (d, J = 5.4 Hz, 1H), 6.90 - 7.02 (m, 3H), 7.30 - 7.37 (m, 2H), 7.42 (s, 1H), 7.46 (d, J = 8.8 Hz, 1H), 7.52 (s, 1H), 7.67 - 7.73 (m, 1H), 8.10 - 8.15 (m, 1H), 8.51 (d, J = 5.4 Hz, 1H), 11.82 - 11.86 (bs, 1H), 12.17 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 552 (M⁺+1)

35 Example 743: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-[(2R)-2-phenylpropanoyl]thiourea

[0853] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available (2R)-2-phenylpropanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and (2R)-2-phenylpropanoyl isothiocyanate was prepared using the resultant (2R)-2-phenylpropanoyl chloride as a starting compound according to the description of the literature. (2R)-2-Phenylpropanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (31 mg, yield 38%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.44 (d, J = 7.1 Hz, 3H), 3.92 (s, 3H), 3.95 (s, 3H), 4.08 - 4.16 (m, 1H), 6.55 (d, J = 5.4 Hz, 1H), 7.24 - 7.45 (m, 8H), 7.50 (s, 1H), 7.72 - 7.78 (m, 2H), 8.52 (d, J = 5.1 Hz, 1H), 11.66 - 11.69 (bs, 1H), 12.41 - 12.44 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 488 (M⁺+1)

50 Example 744: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-[(2R)-2-phenylpropanoyl]thiourea

[0854] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available (2R)-2-phenylpropanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and (2R)-2-phenylpropanoyl isothiocyanate was prepared using the resultant (2R)-2-phenylpropanoyl chloride as a starting compound according to the description of the literature. (2R)-2-Phenylpropanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The

reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (56 mg, yield 71%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.44 (d, J = 6.8 Hz, 3H), 3.94 (s, 3H), 3.96 (s, 3H), 4.08 - 4.16 (m, 1H), 6.42 (d, J = 5.4 Hz, 1H), 7.27 - 7.49 (m, 7H), 7.53 (s, 1H), 7.66 - 7.72 (m, 1H), 8.10 - 8.14 (m, 1H), 8.52 (d, J = 5.1 Hz, 1H), 11.75 - 11.78 (bs, 1H), 12.44 - 12.47 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 522 (M⁺+1)

Example 745: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-phenoxypropanoyl)thiourea

[0855] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-phenoxypropanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-phenoxypropanoyl isothiocyanate was prepared using the resultant 2-phenoxypropanoyl chloride as a starting compound according to the description of the literature. 2-Phenoxypropanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (14 mg, yield 16%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.58 (d, J = 6.6 Hz, 3H), 3.93 (s, 3H), 3.95 (s, 3H), 4.86 - 4.93 (m, 1H), 6.44 (d, J = 5.1 Hz, 1H), 6.96 - 7.01 (m, 3H), 7.21 - 7.35 (m, 4H), 7.39 (s, 1H), 7.50 (s, 1H), 7.75 - 7.80 (m, 2H), 8.46 (d, J = 5.4 Hz, 1H), 10.27 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 504 (M⁺+1)

Example 746: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-phenoxypropanoyl)thiourea

[0856] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-phenoxypropanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-phenoxypropanoyl isothiocyanate was prepared using the resultant 2-phenoxypropanoyl chloride as a starting compound according to the description of the literature. 2-Phenoxypropanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (33 mg, yield 41%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.58 (d, J = 6.6 Hz, 3H), 3.94 (s, 3H), 3.95 (s, 3H), 4.87 - 4.94 (m, 1H), 6.35 (d, J = 5.1 Hz, 1H), 6.88 - 7.53 (m, 8H), 7.69 - 7.74 (m, 1H), 8.07 (d, J = 2.4 Hz, 1H), 8.45 (d, J = 5.4 Hz, 1H), 10.43 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 538 (M⁺+1)

Example 747: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-phenylbutanoyl)thiourea

[0857] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-phenylbutanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-phenylbutanoyl isothiocyanate was prepared using the resultant 2-phenylbutanoyl chloride as a starting compound according to the description of the literature. 2-Phenylbutanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (41 mg, yield 48%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.86 (t, J = 7.3 Hz, 3H), 1.22 - 1.28 (bs, 1H), 1.69 - 1.81 (m, 1H), 2.01 - 2.14 (m, 1H), 3.93 (s, 3H), 3.95 (s, 3H), 6.55 (d, J = 5.4 Hz, 1H), 7.26 - 7.44 (m, 8H), 7.50 (s, 1H), 7.72 - 7.79 (m, 2H), 8.53 (d, J = 5.1 Hz, 1H), 11.69 - 11.72 (bs, 1H), 12.44 - 12.48 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

Example 748: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-phenylbutanoyl)thiourea

[0858] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-phenylbutanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-phenylbutanoyl isothiocyanate was prepared using the resultant 2-phenylbutanoyl chloride as a starting compound according to the description of the literature. 2-Phenylbutanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added

to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (37 mg, yield 46%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.83 - 0.90 (m, 3H), 1.22 - 1.29 (bs, 1H), 1.69 - 1.81 (m, 1H), 2.01 - 2.14 (m, 1H), 3.94 (s, 3H), 3.95 (s, 3H), 6.40 (d, J = 5.1 Hz, 1H), 7.28 - 7.47 (m, 7H), 7.52 (s, 1H), 7.66 - 7.72 (m, 1H), 8.10 - 8.14 (m, 1H), 8.50 (d, J = 5.1 Hz, 1H), 11.77 - 11.80 (bs, 1H), 12.45 - 12.48 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 536 (M⁺+1)

Example 749: N-[(2,2-Dichloro-1-methylcyclopropyl)carbonyl]-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[0859] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2,2-dichloro-1-methyl-1-cyclopropanecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2,2-dichloro-1-methyl-1-cyclopropanecarbonyl isothiocyanate was prepared using the resultant 2,2-dichloro-1-methyl-1-cyclopropanecarbonyl chloride as a starting compound according to the description of the literature. 2,2-Dichloro-1-methyl-1-cyclopropanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (63 mg, yield 73%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.67 (s, 3H), 1.71 (d, J = 8.1 Hz, 1H), 2.13 (d, J = 7.8 Hz, 1H), 3.93 (s, 3H), 3.95 (s, 3H), 6.55 (d, J = 5.1 Hz, 1H), 7.28 - 7.34 (m, 2H), 7.41 (s, 1H), 7.50 (s, 1H), 7.75 - 7.81 (bs, 2H), 8.52 (d, J = 5.1 Hz, 1H), 12.11 - 12.20 (m, 1H)

Mass spectrometry value (ESI-MS, m/z): 506 (M⁺+1)

Example 750: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[(2,2-dichloro-1-methylcyclopropyl)carbonyl]thiourea

[0860] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2,2-dichloro-1-methyl-1-cyclopropanecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2,2-dichloro-1-methyl-1-cyclopropanecarbonyl isothiocyanate was prepared using the resultant 2,2-dichloro-1-methyl-1-cyclopropanecarbonyl chloride as a starting compound according to the description of the literature. 2,2-Dichloro-1-methyl-1-cyclopropanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (27 mg, yield 34%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.67 (s, 3H), 1.72 (d, J = 7.8 Hz, 1H), 2.13 (d, J = 7.8 Hz, 1H), 3.95 (s, 3H), 3.96 (s, 3H), 6.42 (d, J = 4.4 Hz, 1H), 7.43 (s, 1H), 7.48 (d, J = 8.8 Hz, 1H), 7.53 (s, 1H), 7.67 - 7.74 (bs, 1H), 8.13 - 8.18 (bs, 1H), 8.51 (d, J = 5.1 Hz, 1H), 12.19 - 12.23 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 540 (M⁺+1)

Example 751: N-(4-Butoxybenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[0861] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-butoxybenzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-butoxy-1-benzenecarbonyl isothiocyanate was prepared using the resultant 4-butoxy-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 4-Butoxy-1-benzenecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (59 mg, yield 65%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.95 (t, J = 7.6 Hz, 3H), 1.40 - 1.52 (m, 2H), 1.69 - 1.78 (m, 2H), 3.94 (s, 3H), 3.96 (s, 3H), 4.06 - 4.12 (m, 2H), 6.56 (d, J = 5.1 Hz, 1H), 7.05 - 7.11 (m, 2H), 7.30 - 7.36 (m, 2H), 7.42 (s, 1H), 7.51 (s, 1H), 7.80 - 7.87 (m, 2H), 8.00 - 8.05 (m, 2H), 8.52 (d, J = 5.1 Hz, 1H), 11.40 - 11.43 (bs, 1H), 12.72 - 12.76 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 532 (M⁺+1)

Example 752: N-(4-Butoxybenzoyl)-N'-(3-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl)thiourea

[0862] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-butoxybenzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-butoxy-1-benzenecarbonyl isothiocyanate was prepared using the resultant 4-butoxy-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 4-Butoxy-1-benzenecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (55 mg, yield 65%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.92 - 0.99 (m, 3H), 1.40 - 1.52 (m, 2H), 1.69 - 1.79 (m, 2H), 3.95 (s, 3H), 3.96 (s, 3H), 4.06 - 4.12 (m, 2H), 6.43 (d, J = 5.1 Hz, 1H), 7.05 - 7.11 (m, 2H), 7.42 - 7.56 (m, 3H), 7.73 - 7.79 (m, 1H), 8.00 - 8.06 (m, 2H), 8.18 - 8.24 (m, 1H), 8.52 (d, J = 5.4 Hz, 1H), 11.50 - 11.54 (bs, 1H), 12.74 - 12.79 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 566 (M⁺+1)

Example 753: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-[4-(pentyloxy)benzoyl]thiourea

[0863] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-(pentyloxy)benzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-(pentyloxy)-1-benzenecarbonyl isothiocyanate was prepared using the resultant 4-(pentyloxy)-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 4-(Pentyloxy)-1-benzenecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (61 mg, yield 65%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.88 - 0.94 (m, 3H), 1.31 - 1.46 (m, 4H), 1.71 - 1.80 (m, 2H), 3.94 (s, 3H), 3.96 (s, 3H), 4.08 (t, J = 6.3 Hz, 2H), 6.56 (d, J = 5.1 Hz, 1H), 7.04 - 7.10 (m, 2H), 7.30 - 7.36 (m, 2H), 7.42 (s, 1H), 7.51 (s, 1H), 7.80 - 7.87 (m, 2H), 8.00 - 8.05 (m, 2H), 8.52 (d, J = 5.4 Hz, 1H), 11.40 - 11.43 (bs, 1H), 12.73 - 12.76 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 546 (M⁺+1)

Example 754: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[4-(pentyloxy)benzoyl]thiourea

[0864] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-(pentyloxy)benzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-(pentyloxy)-1-benzenecarbonyl isothiocyanate was prepared using the resultant 4-(pentyloxy)-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 4-(Pentyloxy)-1-benzenecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (63 mg, yield 72%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.88 - 0.94 (m, 3H), 1.31 - 1.47 (m, 4H), 1.71 - 1.80 (m, 2H), 3.95 (s, 3H), 3.96 (s, 3H), 4.08 (t, J = 6.6 Hz, 2H), 6.43 (d, J = 5.1 Hz, 1H), 7.05 - 7.10 (m, 2H), 7.43 (s, 1H), 7.50 (d, J = 8.8 Hz, 1H), 7.54 (s, 1H), 7.72 - 7.79 (m, 1H), 8.00 - 8.05 (m, 2H), 8.18 - 8.24 (m, 1H), 8.51 (d, J = 5.1 Hz, 1H), 11.49 - 11.53 (bs, 1H), 12.74 - 12.78 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 580 (M⁺+1)

Example 755: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-[4-(hexyloxy)benzoyl]thiourea

[0865] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-(hexyloxy)benzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-(hexyloxy)-1-benzenecarbonyl isothiocyanate was prepared using the resultant 4-(hexyloxy)-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 4-(Hexyloxy)-1-benzenecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (58 mg, yield 61%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.86 - 0.92 (m, 3H), 1.29 - 1.35 (m, 4H), 1.39 - 1.48 (m, 2H), 1.70 - 1.79 (m, 2H), 3.94 (s, 3H), 3.96 (s, 3H), 4.05 - 4.11 (m, 2H), 6.56 (d, J = 5.1 Hz, 1H), 7.04 - 7.10 (m, 2H), 7.30 - 7.36 (m, 2H),

7.42 (s, 1H), 7.51 (s, 1H), 7.80 - 7.87 (m, 2H), 8.00 - 8.05 (m, 2H), 8.52 (d, J = 5.4 Hz, 1H), 11.39 - 11.43 (bs, 1H), 12.72 - 12.76 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 560 (M⁺+1)

5 Example 756: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[4-(hexyloxy)benzoyl]thiourea

[0866] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-(hexyloxy)benzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-(hexyloxy)-1-benzenecarbonyl isothiocyanate was prepared using the resultant 4-(hexyloxy)-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 4-(Hexyloxy)-1-benzenecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (56 mg, yield 63%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.86 - 0.91 (m, 3H), 1.28 - 1.35 (m, 4H), 1.39 - 1.47 (m, 2H), 1.70 - 1.79 (m, 2H), 3.95 (s, 3H), 3.96 (s, 3H), 4.08 (t, J = 6.3 Hz, 2H), 6.43 (d, J = 5.1 Hz, 1H), 7.05 - 7.10 (m, 2H), 7.43 (s, 1H), 7.50 (d, J = 9.0 Hz, 1H), 7.54 (s, 1H), 7.72 - 7.78 (m, 1H), 8.00 - 8.05 (m, 2H), 8.18 - 8.25 (m, 1H), 8.51 (d, J = 5.1 Hz, 1H), 11.49 - 11.52 (bs, 1H), 12.73 - 12.77 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 595 (M⁺+1)

20 Example 757: N-[2-(4-Chlorophenoxy)-2-methylpropanoyl]-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]thiourea

[0867] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(4-chlorophenoxy)-2-methylpropanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(4-chlorophenoxy)-2-methylpropanoyl isothiocyanate was prepared using the resultant 2-(4-chlorophenoxy)-2-methylpropanoyl chloride as a starting compound according to the description of the literature. 2-(4-Chlorophenoxy)-2-methylpropanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (39 mg, yield 41%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.56 (s, 6H), 3.93 (s, 3H), 3.96 (s, 3H), 6.56 (d, J = 5.1 Hz, 1H), 7.07 - 7.13 (m, 2H), 7.31 - 7.53 (m, 6H), 7.78 - 7.85 (m, 2H), 8.53 (d, J = 5.1 Hz, 1H), 10.54 - 10.57 (bs, 1H), 12.10 - 12.15 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 552 (M⁺+1)

35 Example 758: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[2-(4-chlorophenoxy)-2-methylpropanoyl]thiourea

[0868] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(4-chlorophenoxy)-2-methylpropanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(4-chlorophenoxy)-2-methylpropanoyl isothiocyanate was prepared using the resultant 2-(4-chlorophenoxy)-2-methylpropanoyl chloride as a starting compound according to the description of the literature. 2-(4-Chlorophenoxy)-2-methylpropanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (17 mg, yield 19%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.56 (s, 6H), 3.95 (s, 3H), 3.96 (s, 3H), 6.42 (d, J = 5.1 Hz, 1H), 7.07 - 7.12 (m, 2H), 7.38 - 7.55 (m, 5H), 7.71 - 7.78 (m, 1H), 8.13 - 8.19 (m, 1H), 8.52 (d, J = 5.1 Hz, 1H), 10.67 - 10.71 (bs, 1H), 12.13 - 12.17 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 587 (M⁺+1)

50 Example 759: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2,2,3,3-tetramethylcyclopropyl)carbonyl]thiourea

[0869] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2,2,3,3-tetramethylcyclopropanecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2,2,3,3-tetramethyl-1-cyclopropanecarbonyl isothiocyanate was prepared using the resultant 2,2,3,3-tetramethyl-1-cyclopropanecarbonyl chloride as a starting compound according to the description of the literature. 2,2,3,3-Tetramethyl-1-cyclopropanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare

a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (11 mg, yield 14%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.20 (s, 6H), 1.27 (s, 6H), 1.73 (s, 1H), 3.93 (s, 3H), 3.95 (s, 3H), 6.54 (d, J = 5.4 Hz, 1H), 7.26 - 7.32 (m, 2H), 7.41 (s, 1H), 7.50 (s, 1H), 7.73 - 7.80 (m, 2H), 8.51 (d, J = 5.1 Hz, 1H), 11.41 - 11.45 (bs, 1H), 12.55 - 12.59 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 480 (M⁺+1)

Example 760: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2,2,3,3-tetramethylcyclopropyl)carbonyl]thiourea

[0870] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2,2,3,3-tetramethylcyclopropanecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2,2,3,3-tetramethyl-1-cyclopropanecarbonyl isothiocyanate was prepared using the resultant 2,2,3,3-tetramethyl-1-cyclopropanecarbonyl chloride as a starting compound according to the description of the literature. 2,2,3,3-Tetramethyl-1-cyclopropanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (17 mg, yield 21%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.21 (s, 6H), 1.27 (s, 6H), 1.71 - 1.75 (m, 1H), 3.95 (s, 3H), 3.96 (s, 3H), 6.41 (d, J = 5.1 Hz, 1H), 7.43 (s, 1H), 7.46 (d, J = 8.5 Hz, 1H), 7.53 (s, 1H), 7.66 - 7.72 (m, 1H), 8.12 - 8.18 (m, 1H), 8.51 (d, J = 5.1 Hz, 1H), 11.50 - 11.53 (bs, 1H), 12.59 (d, J = 4.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 514 (M⁺+1)

Example 761: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-methoxy-2-phenylacetyl)thiourea

[0871] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-methoxy-2-phenylacetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-methoxy-2-phenylethanoyl isothiocyanate was prepared using the resultant 2-methoxy-2-phenylethanoyl chloride as a starting compound according to the description of the literature. 2-Methoxy-2-phenylethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (25 mg, yield 30%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.40 (s, 3H), 3.93 (s, 3H), 3.94 (s, 3H), 4.54 (s, 1H), 4.87 (s, 1H), 6.43 (d, J = 5.1 Hz, 1H), 7.20 - 7.54 (m, 9H), 7.80 - 7.86 (m, 2H), 8.45 (d, J = 5.1 Hz, 1H), 10.20 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 503 (M⁺+1)

Example 762: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-methoxy-2-phenylacetyl)thiourea

[0872] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-methoxy-2-phenylacetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-methoxy-2-phenylethanoyl isothiocyanate was prepared using the resultant 2-methoxy-2-phenylethanoyl chloride as a starting compound according to the description of the literature. 2-Methoxy-2-phenylethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (28 mg, yield 35%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.40 (s, 3H), 3.94 (s, 3H), 3.95 (s, 3H), 4.54 (s, 1H), 4.88 (s, 1H), 6.33 (d, J = 5.1 Hz, 1H), 7.28 - 7.55 (m, 8H), 7.77 - 7.83 (m, 1H), 8.11 - 8.16 (m, 1H), 8.44 (d, J = 5.1 Hz, 1H), 10.37 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 537 (M⁺+1)

Example 763: N-[2-(2-Chlorophenoxy)propanoyl]-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[0873] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-chlorophenoxy)propanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and

2-(2-chlorophenoxy)propanoyl isothiocyanate was prepared using the resultant 2-(2-chlorophenoxy)propanoyl chloride as a starting compound according to the description of the literature. 2-(2-Chlorophenoxy)propanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (4 mg, yield 5%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.62 (d, J = 6.6 Hz, 3H), 3.93 (s, 3H), 3.95 (s, 3H), 4.96 (q, J = 6.6 Hz, 1H), 6.46 (d, J = 5.1 Hz, 1H), 6.98 - 7.52 (m, 8H), 7.74 - 7.79 (m, 2H), 8.47 (d, J = 5.1 Hz, 1H), 10.31 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 537 (M⁺+1)

Example 764: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[2-(2-chlorophenoxy)propanoyl]thiourea

[0874] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-chlorophenoxy)propanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-chlorophenoxy)propanoyl isothiocyanate was prepared using the resultant 2-(2-chlorophenoxy)propanoyl chloride as a starting compound according to the description of the literature. 2-(2-Chlorophenoxy)propanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (53 mg, yield 62%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.62 (d, J = 6.8 Hz, 3H), 3.95 (s, 3H), 3.95 (s, 3H), 4.93 - 5.01 (m, 1H), 6.37 (d, J = 5.4 Hz, 1H), 6.95 - 7.55 (m, 8H), 7.67 - 7.71 (m, 1H), 8.07 (s, 1H), 8.47 (d, J = 5.4 Hz, 1H), 10.50 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 572 (M⁺+1)

Example 765: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-tetrahydro-2-furanylcarbonylthiourea

[0875] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available tetrahydro-2-furancarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and tetrahydro-2-furancarboxyl isothiocyanate was prepared using the resultant tetrahydro-2-furancarboxyl chloride as a starting compound according to the description of the literature. Tetrahydro-2-furancarboxyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (5 mg, yield 6%).

¹H-NMR (DMSO-d₆, 400 MHz) : δ 1.84 - 1.92 (m, 2H), 1.97 - 2.06 (m, 1H), 2.17 - 2.27 (m, 1H), 3.82 - 3.88 (m, 1H), 3.94 (s, 3H), 3.95 (s, 3H), 3.97 - 4.04 (m, 1H), 4.39 - 4.44 (m, 1H), 6.45 (d, J = 5.1 Hz, 1H), 7.21 - 7.26 (m, 2H), 7.40 (s, 1H), 7.52 (s, 1H), 7.84 (d, J = 9.0 Hz, 2H), 8.48 (d, J = 5.4 Hz, 1H), 9.83 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 454 (M⁺+1)

Example 766: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-tetrahydro-2-furanylcarbonylthiourea

[0876] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available tetrahydro-2-furancarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and tetrahydro-2-furancarboxyl isothiocyanate was prepared using the resultant tetrahydro-2-furancarboxyl chloride as a starting compound according to the description of the literature. Tetrahydro-2-furancarboxyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (5 mg, yield 7%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.84 - 1.92 (m, 2H), 1.97 - 2.06 (m, 1H), 2.17 - 2.27 (m, 1H), 3.83 - 3.89 (m, 1H), 3.95 (s, 3H), 3.96 (s, 3H), 3.97 - 4.03 (m, 1H), 4.41 - 4.46 (m, 1H), 6.38 (d, J = 5.4 Hz, 1H), 7.42 (s, 1H), 7.44 (s, 1H), 7.55 (s, 1H), 7.79 - 7.84 (m, 1H), 8.15 (d, J = 2.4 Hz, 1H), 8.49 (d, J = 5.4 Hz, 1H), 10.01 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 488 (M⁺+1)

Example 767: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-[(3-methoxycyclohexyl)carbonyl]thiourea

[0877] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-methoxy-1-cyclohexanecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and

3-methoxy-1-cyclohexanecarbonyl isothiocyanate was prepared using the resultant 3-methoxy-1-cyclohexanecarbonyl chloride as a starting compound according to the description of the literature. 3-Methoxy-1-cyclohexanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (38 mg, yield 45%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.32 - 1.61 (m, 5H), 1.73 - 1.85 (m, 2H), 1.90 - 1.97 (m, 1H), 2.85 - 2.94 (m, 1H), 3.25 (s, 3H), 3.53 - 3.58 (bs, 1H), 3.93 (s, 3H), 3.96 (s, 3H), 6.56 (d, J = 5.1 Hz, 1H), 7.30 (d, J = 8.8 Hz, 2H), 7.41 (s, 1H), 7.51 (s, 1H), 7.74 - 7.80 (m, 2H), 8.53 (d, J = 5.4 Hz, 1H), 11.48 - 11.51 (bs, 1H), 12.57 (d, J = 4.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 496 (M⁺+1)

Example 768: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[(3-methoxycyclohexyl)carbonyl]thiourea

[0878] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-methoxy-1-cyclohexanecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-methoxy-1-cyclohexanecarbonyl isothiocyanate was prepared using the resultant 3-methoxy-1-cyclohexanecarbonyl chloride as a starting compound according to the description of the literature. 3-Methoxy-1-cyclohexanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (31 mg, yield 39%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.33 - 1.61 (m, 5H), 1.73 - 1.85 (m, 2H), 1.90 - 1.97 (m, 1H), 2.85 - 2.94 (m, 1H), 3.25 (s, 3H), 3.53 - 3.57 (bs, 1H), 3.95 (s, 3H), 3.96 (s, 3H), 6.43 (d, J = 5.1 Hz, 1H), 7.43 (s, 1H), 7.48 (d, J = 8.8 Hz, 1H), 7.54 (s, 1H), 7.67 - 7.72 (m, 1H), 8.14 - 8.18 (m, 1H), 8.53 (d, J = 5.4 Hz, 1H), 11.59 (d, J = 2.9 Hz, 1H), 12.59 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 530 (M⁺+1)

Example 769: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2-ethoxyacetyl)thiourea

[0879] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-ethoxyacetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-ethoxyethanoyl isothiocyanate was prepared using the resultant 2-ethoxyethanoyl chloride as a starting compound according to the description of the literature. 2-Ethoxyethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (9 mg, yield 13%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.21 (t, J = 7.1 Hz, 3H), 3.55 - 3.62 (m, 2H), 3.96 (s, 3H), 3.97 (s, 3H), 4.06 (s, 2H), 6.54 (d, J = 5.4 Hz, 1H), 7.26 (d, J = 8.8 Hz, 2H), 7.42 (s, 1H), 7.56 (s, 1H), 7.82 (d, J = 9.0 Hz, 2H), 8.54 (d, J = 5.6 Hz, 1H), 9.87 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : (M⁺+1)

Example 770: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2-[(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl]oxy)acetyl)thiourea

[0880] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-[(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl]oxy}acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-[(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl]oxy}ethanoyl isothiocyanate was prepared using the resultant 2-[(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl]oxy}ethanoyl chloride as a starting compound according to the description of the literature. 2-[(1R,2S,5R)-2-Isopropyl-5-methylcyclohexyl]oxy}ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (27 mg, yield 29%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.77 (d, J = 6.8 Hz, 3H), 0.81 - 1.00 (m, 9H), 1.23 - 1.40 (m, 1H), 1.56 - 1.67 (m, 2H), 2.09 - 2.15 (m, 1H), 2.24 - 2.34 (m, 1H), 3.94 (s, 3H), 3.95 (s, 3H), 4.02 - 4.16 (m, 2H), 6.47 (d, J = 5.4 Hz, 1H), 7.22 - 7.27 (m, 2H), 7.40 (s, 1H), 7.52 (s, 1H), 7.76 - 7.81 (m, 2H), 8.48 (d, J = 5.4 Hz, 1H), 9.72 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 551 (M⁺+1)

Example 771: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-[(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl]oxy)acetylthiourea

[0881] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-[(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl]oxy}acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-[(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl]oxy}ethanoyl isothiocyanate was prepared using the resultant 2-[(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl]oxy}ethanoyl chloride as a starting compound according to the description of the literature. 2-[(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl]oxy}ethanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (17 mg, yield 19%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.77 (d, J = 6.8 Hz, 3H), 0.80 - 1.02 (m, 9H), 1.23 - 1.40 (m, 1H), 1.56 - 1.67 (m, 2H), 2.08 - 2.14 (m, 1H), 2.23 - 2.34 (m, 1H), 3.95 (s, 3H), 3.96 (s, 3H), 4.04 - 4.18 (m, 2H), 6.36 (d, J = 5.1 Hz, 1H), 7.41 (s, 1H), 7.43 (d, J = 8.8 Hz, 1H), 7.54 (s, 1H), 7.70 - 7.74 (m, 1H), 8.09 (d, J = 2.4 Hz, 1H), 8.48 (d, J = 5.1 Hz, 1H), 9.93 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 585 (M⁺+1)

Example 772: 4-[(6,7-Dimethoxy-4-quinazolinyloxy)phenyl benzoate

[0882] Chlorobenzene (7 ml) was added to 4-chloro-6,7-dimethoxyquinazoline (2.5 g) and 4-hydroxyphenyl benzoate (4.78 g), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. Methanol was added to the residue, and the precipitated crystal was collected by filtration and was washed to give the title compound (3.49 g, yield 78%).

¹H-NMR (chloroform-d, 400 MHz): δ 4.10 (s, 3H), 4.10 (s, 3H), 7.31 - 7.38 (m, 4H), 7.49 (s, 1H), 7.51 - 7.59 (m, 3H), 7.64 - 7.69 (m, 1H), 8.20 - 8.25 (m, 2H), 8.68 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 403 (M⁺+1)

Example 773: 4-[(6,7-Dimethoxy-4-quinazolinyloxy)phenol

[0883] Methanol (5 ml) and sodium hydroxide (0.2 g) were added to 4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl benzoate (500 mg), and the mixture was stirred at 0°C for 30 min. A saturated aqueous ammonium chloride solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. Methanol was added to the residue, and the precipitated crystal was collected by filtration and was washed to give the title compound (350 mg, yield 95%).

¹H-NMR (chloroform-d, 400 MHz): δ 4.08 (s, 3H), 4.11 (s, 3H), 6.91 - 6.95 (m, 2H), 7.05 - 7.10 (m, 2H), 7.57 (s, 1H), 7.59 (s, 1H), 8.66 (s, 1H)

Mass spectrometry value (FD-MS, m/z): 298 (M⁺)

Example 774: Methyl 2-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenoxy]acetate

[0884] 4-[(6,7-Dimethoxy-4-quinazolinyloxy)phenol (100 mg) was dissolved in dimethylformamide (2 ml) to prepare a solution. Sodium hydride (15 mg) was added to the solution, and the mixture was stirred at 0°C for 10 min. Methyl-bromoacetate (0.037 ml) was added thereto, and the mixture was further stirred at 0°C for 30 min. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with ethyl acetate, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. Diethyl ether was added to the residue, and the precipitated crystal was collected by filtration and was washed to give the title compound (88 mg, yield 71%).

¹H-NMR (chloroform-d, 400 MHz): δ 3.84 (s, 3H), 4.07 (s, 6H), 4.67 (s, 2H), 6.99 - 7.04 (m, 2H), 7.17 - 7.21 (m, 2H), 7.33 (s, 1H), 7.55 (s, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 371 (M⁺+1)

Example 775: 2-{4-[(6,7-Dimethoxy-4-quinazolinyloxy)phenoxy]acetic acid

[0885] Methyl 2-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenol (70 mg) was dissolved in methanol (1 ml) to prepare a

solution. A solution of sodium hydroxide (70 mg) in water was added to the solution, and the mixture was stirred at 0°C for 2 hr. Concentrated hydrochloric acid was added to the reaction solution, and the precipitated crystal was collected by filtration and was washed with methanol, diethyl ether, and hexane to give the title compound (65 mg, yield 97%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.98 (s, 3H), 3.99 (s, 3H), 4.73 (s, 2H), 6.97 - 7.02 (m, 2H), 7.20 - 7.25 (m, 2H), 7.39 (s, 1H), 7.56 (s, 1H), 8.56 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 357 (M⁺+1)

Example 776: N1-(2-Methoxyphenyl)-2-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenoxy}acetamide

[0886] 2-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenoxy}acetic acid (150 mg), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (WSC · HCl) (122 mg), and 1-hydroxybenzotriazole hydrate (HOBT · H₂O) (86 mg) were dissolved in chloroform (5 ml) to prepare a solution. o-Anisidine (63 mg) was then added to the solution, and the mixture was heated under reflux for 3 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The chloroform layer was washed with 1 N hydrochloric acid, water, and saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (155 mg, yield 80%).

[0887] The compound (50 mg) thus obtained was dissolved in 10% hydrochloric acid-methanol solution (6 ml), and the solution was allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 49 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.88 (s, 3H), 4.04 (s, 3H), 4.05 (s, 3H), 4.77 (s, 1H), 4.86 (s, 1H), 6.80 - 6.83 (m, 1H), 6.93 - 6.97 (m, 1H), 7.09 - 7.42 (m, 6H), 7.64 (s, 1H), 7.75 (d, J = 2.7 Hz, 1H), 8.05 - 8.09 (m, 1H), 8.79 - 8.82 (m, 1H), 9.29 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 461 (M⁺+1)

Example 777: N-(2-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenoxy}ethyl)-N-(2-methoxyphenyl)amine

[0888] N1-(2-Methoxyphenyl)-2-(4-[(6,7-dimethoxy-4-quinolyl)oxy]phenoxy)acetamide (100 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A borane-tetrahydrofuran complex (1.0 M solution: 1.08 ml) was then added to the solution, and the mixture was heated under reflux for 5 hr. 1 N Hydrochloric acid was added thereto, and the mixture was further heated under reflux for 30 min. A 5% aqueous sodium hydroxide solution was added to the reaction solution, the mixture was extracted with chloroform, and the extract was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (58 mg, yield 60%).

[0889] The resultant compound (55 mg) was dissolved in 10% hydrochloric acid-methanol solution (4 ml) to prepare a solution which was then allowed to stand at room temperature for 20 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 55 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.53 (t, J = 5.4 Hz, 2H), 3.80 (s, 3H), 4.04 (s, 3H), 4.05 (s, 3H), 4.23 (t, J = 5.6 Hz, 2H), 6.66 - 6.72 (m, 1H), 6.75 - 6.91 (m, 4H), 7.18 (d, J = 9.0 Hz, 2H), 7.36 (d, J = 9.0 Hz, 2H), 7.63 (s, 1H), 7.76 (s, 1H), 8.80 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 447 (M⁺+1)

Example 778: N1-(3-Methoxyphenyl)-2-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenoxy}acetamide

[0890] 2-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenoxy}acetic acid (150 mg), WSC · HCl (122 mg), and HOBT · H₂O (86 mg) were dissolved in chloroform (5 ml) to prepare a solution. m-Anisidine (63 mg) was then added to the solution, and the mixture was heated under reflux for 3 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The chloroform layer was washed with 1 N hydrochloric acid, water, and saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (173 mg, yield 89%).

[0891] The resultant compound (45 mg) was dissolved in 10% hydrochloric acid-methanol solution (4 ml) to prepare a solution which was then allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 42 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.74 (s, 3H), 4.04 (s, 3H), 4.05 (s, 3H), 4.77 (s, 1H), 4.80 (s, 1H), 6.67 - 6.70 (m, 1H), 6.80 - 6.83 (m, 1H), 7.13 - 7.40 (m, 7H), 7.62 (s, 1H), 7.75 (s, 1H), 8.80 (d, J = 6.8 Hz, 1H), 10.20 (s, 1H)
Mass spectrometry value (ESI-MS, m/z) : 461 (M⁺+1)

5 Example 779: N-(2-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenoxy}ethyl)-N-(3-methoxyphenyl)amine

[0892] N1-(3-Methoxyphenyl)-2-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenoxy}acetamide (112 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A borane-tetrahydrofuran complex (1.0 M solution: 1.22 ml) was then added to the solution, and the mixture was heated under reflux for 5 hr. 1 N Hydrochloric acid was added thereto, and the mixture was further heated under reflux for 30 min. A 5% aqueous sodium hydroxide solution was added to the reaction solution, the mixture was extracted with chloroform, and the extract was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (64 mg, yield 59%).

[0893] The resultant compound (60 mg) was dissolved in a 10% hydrochloric acid-methanol solution (4 ml) to prepare a solution which was then allowed to stand at room temperature for 20 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 58 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.59 (t, J = 5.1 Hz, 2H), 3.73 (s, 3H), 4.04 (s, 6H), 4.26 (t, J = 5.1 Hz, 2H), 6.53 - 6.70 (m, 3H), 6.80 (d, J = 6.8 Hz, 1H), 7.15 - 7.22 (m, 3H), 7.35 - 7.40 (m, 2H), 7.76 (d, J = 5.1 Hz, 2H), 8.81 (d, J = 6.8 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 447 (M⁺+1)

Example 780: N1-(4-Methoxyphenyl)-2-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenoxy}acetamide

[0894] 2-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenoxy}acetic acid (150 mg), WSC · HCl (122 mg), and HOBT · H₂O (86 mg) were dissolved in chloroform (5 ml) to prepare a solution. p-Anisidine (63 mg) was then added to the solution, and the mixture was heated under reflux for 4 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The chloroform layer was washed with 1 N hydrochloric acid, water, and saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (147 mg, yield 76%).

[0895] The resultant compound (47 mg) was dissolved in a 10% hydrochloric acid-methanol solution (6 ml) which was then allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 49 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.73 (s, 3H), 4.03 (s, 3H), 4.04 (s, 3H), 4.76 (s, 2H), 6.80 (d, J = 6.8 Hz, 1H), 6.90 - 6.92 (m, 2H), 7.12 - 7.40 (m, 4H), 7.55 - 7.63 (m, 3H), 7.74 (s, 1H), 8.79 (d, J = 6.6 Hz, 1H), 10.05 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 461 (M⁺+1)

40 Example 781: N-(2-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenoxy}ethyl)-N-(4-methoxyphenyl)amine

[0896] N1-(4-Methoxyphenyl)-2-(4-[(6,7-dimethoxy-4-quinolyl)oxy]phenoxy}acetamide (90 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A borane-tetrahydrofuran complex (1.0 M solution: 0.98 ml) was then added to the solution, and the mixture was heated under reflux for 3 hr. 1 N Hydrochloric acid was added thereto, and the mixture was further heated under reflux for 30 min. A 5% aqueous sodium hydroxide solution was added to the reaction solution, the mixture was extracted with chloroform, and the extract was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (52 mg, yield 60%).

[0897] The resultant compound (52 mg) was dissolved in a 10% hydrochloric acid-methanol solution (4 ml) to prepare a solution which was then allowed to stand at room temperature for 20 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 42 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.54 - 3.62 (m, 2H), 3.70 - 3.74 (m, 3H), 4.04 (s, 3H), 4.04 (s, 3H), 4.21 - 4.26 (m, 2H), 6.81 (d, J = 6.6 Hz, 1H), 6.87 - 6.97 (m, 2H), 7.12 - 7.21 (m, 2H), 7.35 - 7.39 (m, 2H), 7.57 - 7.63 (m, 2H), 7.75 (s, 2H), 8.80 (d, J = 6.8 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 447 (M⁺+1)

Example 782: N1-(2-Methylphenyl)-2-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenoxy}acetamide

[0898] 2-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenoxy}acetic acid (150 mg), WSC·HCl (122 mg), and HOBT·H₂O (86 mg) were dissolved in chloroform (5 ml) to prepare a solution. o-Toluidine (0.055 ml) was then added to the solution, and the mixture was heated under reflux for 6 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (103 mg, yield 55%).

[0899] The resultant compound (101 mg) was dissolved in a 10% hydrochloric acid-methanol solution (4 ml) to prepare a solution which was then allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 100 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.20 (s, 3H), 4.04 (s, 3H), 4.05 (s, 3H), 4.77 (s, 1H), 4.83 (s, 1H), 6.79 - 6.83 (m, 1H), 7.11 - 7.46 (m, 8H), 7.63 - 7.69 (m, 1H), 7.76 (s, 1H), 7.76 (s, 1H), 8.82 (d, J = 6.6 Hz, 1H), 9.60 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 445 (M⁺+1)

Example 783: N-(2-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenoxy}ethyl)-N-(2-methylphenyl)amine

[0900] N1-(2-Methylphenyl)-2-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenoxy}acetamide (65 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A borane-tetrahydrofuran complex (1.0 M solution: 0.74 ml) was then added to the solution, and the mixture was heated under reflux overnight. 1 N Hydrochloric acid was added thereto, and the mixture was further heated under reflux for 30 min. A 5% aqueous sodium hydroxide solution was added to the reaction solution, the mixture was extracted with chloroform, and the extract was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (29 mg, yield 46%).

[0901] The resultant compound (29 mg) was dissolved in a 10% hydrochloric acid-methanol solution (3 ml) to prepare a solution which was then allowed to stand at room temperature for 20 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 30 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.16 (s, 3H), 3.57 (t, J = 5.9 Hz, 2H), 4.04 (s, 3H), 4.05 (s, 3H), 4.25 (t, J = 5.6 Hz, 2H), 6.63 - 6.70 (m, 1H), 6.77 - 6.84 (m, 2H), 7.02 - 7.12 (m, 2H), 7.16 - 7.21 (m, 2H), 7.34 - 7.39 (m, 2H), 7.66 (s, 1H), 7.76 (s, 1H), 8.80 (d, J = 6.8 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 431 (M⁺+1)

Example 784: N1-(3-Methylphenyl)-2-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenoxy}acetamide

[0902] 2-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenoxy}acetic acid (150 mg), WSC · HCl (122 mg), and HOBT · H₂O (86 mg) were dissolved in chloroform (5 ml) to prepare a solution. m-Toluidine (0.055 ml) was then added to the solution, and the mixture was heated under reflux for 4 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The chloroform layer was washed with 1 N hydrochloric acid, water, and saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (102 mg, yield 55%).

[0903] The resultant compound (30 mg) was dissolved in a 10% hydrochloric acid-methanol solution (3 ml) to prepare a solution which was then allowed to stand at room temperature for 20 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 27 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.29 (s, 3H), 4.03 (s, 3H), 4.05 (s, 3H), 4.76 (s, 1H), 4.79 (s, 1H), 6.78 - 6.83 (m, 1H), 6.89 - 6.93 (m, 1H), 7.01 - 7.51 (m, 7H), 7.61 (s, 1H), 7.75 (s, 1H), 8.79 (d, J = 6.6 Hz, 1H), 10.12 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 445 (M⁺+1)

Example 785: N-(2-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenoxy}ethyl)-N-(3-methylphenyl)amine

[0904] N1-(3-Methylphenyl)-2-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenoxy}acetamide (70 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A borane-tetrahydrofuran complex (1.0 M solution: 0.78 ml) was then added to the solution, and the mixture was heated under reflux overnight. 1 N Hydrochloric acid was added thereto, and the mixture was further heated under reflux for 30 min. A 5% aqueous sodium hydroxide solution was added to the reaction

solution, the mixture was extracted with chloroform, and the extract was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (31 mg, yield 46%).

[0905] The resultant compound (31 mg) was dissolved in a 10% hydrochloric acid-methanol solution (3 ml) to prepare a solution which was then allowed to stand at room temperature for 20 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 31 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.23 (s, 3H), 3.49 - 3.53 (m, 2H), 4.04 (s, 3H), 4.05 (s, 3H), 4.20 (t, J = 5.1 Hz, 2H), 6.53 - 6.60 (m, 1H), 6.60 - 6.70 (m, 1H), 6.81 (s, 1H), 6.82 (s, 1H), 7.03 - 7.10 (m, 1H), 7.15 - 7.20 (m, 2H), 7.34 - 7.39 (m, 2H), 7.64 (s, 1H), 7.76 (s, 1H), 8.81 (d, J = 6.8 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 431 (M⁺+1)

Example 786: N1-(4-Methylphenyl)-2-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenoxy}acetamide

[0906] 2-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenoxy}acetic acid (150 mg), WSC · HCl (122 mg), and HOBT · H₂O (86 mg) were dissolved in chloroform (5 ml) to prepare a solution. p-Toluidine (0.055 ml) was then added to the solution, and the mixture was heated under reflux for 3 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The chloroform layer was washed with 1 N hydrochloric acid, water, and saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (76 mg, yield 41%).

[0907] The resultant compound (20 mg) was dissolved in a 10% hydrochloric acid-methanol solution (3 ml) to prepare a solution which was then allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 16 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.27 (s, 3H), 4.03 (s, 3H), 4.04 (s, 3H), 4.76 (s, 1H), 4.78 (s, 1H), 6.78 - 6.82 (m, 1H), 7.12 - 7.16 (m, 2H), 7.19 - 7.25 (m, 2H), 7.36 - 7.40 (m, 2H), 7.52 - 7.57 (m, 2H), 7.63 (s, 1H), 7.74 (s, 1H), 8.79 (d, J = 6.6 Hz, 1H), 10.13 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 445 (M⁺+1)

Example 787: N-(2-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenoxy}ethyl)-N-(4-methylphenyl)amine

[0908] N1-(4-Methylphenyl)-2-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenoxy}acetamide (54 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A borane-tetrahydrofuran complex (1.0 M solution: 0.60 ml) was then added to the solution, and the mixture was heated under reflux for 3 hr. 1 N Hydrochloric acid was added thereto, and the mixture was further heated under reflux for 30 min. A 5% aqueous sodium hydroxide solution was added to the reaction solution, the mixture was extracted with chloroform, and the extract was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (11 mg, yield 20%).

[0909] The resultant compound (11 mg) was dissolved in a 10% hydrochloric acid-methanol solution (3 ml) to prepare a solution which was then allowed to stand at room temperature for 20 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 11 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.24 (s, 3H), 3.54 - 3.60 (m, 2H), 4.04 (s, 3H), 4.05 (s, 3H), 4.16 - 4.27 (m, 2H), 6.81 (d, J = 6.6 Hz, 1H), 6.74 - 7.28 (m, 4H), 7.32 - 7.42 (m, 2H), 7.68 - 7.79 (m, 2H), 7.67 (s, 1H), 7.76 (s, 1H), 8.80 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 431 (M⁺+1)

Example 788: N1-(3-Chlorophenyl)-2-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenoxy}acetamide

[0910] 2-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenoxy}acetic acid (150 mg), WSC · HCl (122 mg), and HOBT · H₂O (86 mg) were dissolved in chloroform (5 ml) to prepare a solution. m-Chloroaniline (65 mg) was then added to the solution, and the mixture was heated under reflux for 3 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The chloroform layer was washed with 1 N hydrochloric acid, water, and saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (141 mg, yield 72%).

[0911] The resultant compound (50 mg) was dissolved in a 10% hydrochloric acid-methanol solution (3 ml) to prepare

a solution which was then allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 40 mg of a hydrochloride.

Mass spectrometry value (ESI-MS, m/z): 465 ($M^+ + 1$)

Example 789: N1-(4-Chlorophenyl)-2-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenoxy}acetamide

[0912] 2-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenoxy}acetic acid (150 mg), WSC · HCl (122 mg), and HOBT · H₂O (86 mg) were dissolved in chloroform (5 ml) to prepare a solution. 4-Chloroaniline (65 mg) was then added to the solution, and the mixture was heated under reflux for 5 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The chloroform layer was washed with 1 N hydrochloric acid, water, and saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (156 mg, yield 79%).

[0913] The resultant compound (49 mg) was dissolved in a 10% hydrochloric acid-methanol solution (3 ml) to prepare a solution which was then allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 39 mg of a hydrochloride.

Mass spectrometry value (ESI-MS, m/z) : 465 ($M^+ + 1$)

Example 790: 6,7-Dimethoxy-4-{4-[3-(4-methylphenoxy)propoxy]phenoxy}quinoline

[0914] p-Cresol (300 mg) was dissolved in acetone (5 ml) to prepare a solution. 1,3-Dibromopropane (0.85 ml), potassium carbonate (765 mg), and tetra-n-butylammonium iodide (102 mg) were then added to the solution, and the mixture was heated under reflux for 3 hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(3-bromopropyl)-4-methylbenzene (1) (466 mg, yield 74%).

[0915] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenol (100 mg) was dissolved in dimethylformamide (2 ml) to prepare a solution. Sodium hydride (16 mg) was then added to the solution, and the mixture was stirred at room temperature for 10 min. A solution of the compound (1) (85 mg) in dimethylformamide was added thereto, and the mixture was further stirred at room temperature for 4 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with ethyl acetate, followed by washing three times with saturated brine. The extract was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (142 mg, yield 95%).

[0916] The resultant compound (138 mg) was dissolved in a 10% hydrochloric acid-methanol solution (5 ml) to prepare a solution which was then allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 117 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.16 - 2.22 (m, 2H), 2.23 (s, 3H), 4.03 (s, 3H), 4.04 (s, 3H), 4.12 (t, J = 6.1 Hz, 2H), 4.20 (t, J = 6.1 Hz, 2H), 6.80 (d, J = 6.3 Hz, 1H), 6.83 - 6.88 (m, 2H), 7.09 (d, J = 8.5 Hz, 2H), 7.14 - 7.20 (m, 2H), 7.31 - 7.36 (m, 2H), 7.59 (s, 1H), 7.74 (s, 1H), 8.77 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 446 ($M^+ + 1$)

Example 791: 6,7-Dimethoxy-4-{4-[3-(3-methylphenoxy)propoxy]phenoxy}quinoline

[0917] m-Cresol (300 mg) was dissolved in acetone (5 ml) to prepare a solution. 1,3-Dibromopropane (0.85 ml), potassium carbonate (765 mg), and tetra-n-butylammonium iodide (102 mg) were then added to the solution, and the mixture was heated under reflux for 3 hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(3-bromopropyl)-3-methylbenzene (1) (490 mg, yield 78%).

[0918] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenol (100 mg) was dissolved in dimethylformamide (2 ml) to prepare a solution. Sodium hydride (16 mg) was then added to the solution, and the mixture was stirred at room temperature for 10 min. A solution of the compound (1) (85 mg) in dimethylformamide was added thereto, and the mixture was further stirred at room temperature for 4 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with ethyl acetate, followed by washing three times with saturated brine. The

extract was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (145 mg, yield 97%).

[0919] The resultant compound (139 mg) was dissolved in a 10% hydrochloric acid-methanol solution (5 ml) to prepare a solution which was then allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 103 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.16 - 2.24 (m, 2H), 2.28 (s, 3H), 4.03 (s, 3H), 4.04 (s, 3H), 4.14 (t, J = 6.3 Hz, 2H), 4.20 (t, J = 6.1 Hz, 2H), 6.74 - 6.81 (m, 4H), 7.14 - 7.20 (m, 3H), 7.32 - 7.37 (m, 2H), 7.58 (s, 1H), 7.74 (s, 1H), 8.77 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 446 (M⁺+1)

Example 792: 6,7-Dimethoxy-4-{4-[3-(2-methylphenoxy)propoxy]phenoxy}quinoline

[0920] o-Cresol (300 mg) was dissolved in acetone (5 ml) to prepare a solution. 1,3-Dibromopropane (0.85 ml), potassium carbonate (765 mg), and tetra-n-butylammonium iodide (102 mg) were added to the solution, and the mixture was heated under reflux for 4 hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(3-bromopropyl)-2-methylbenzene (1) (363 mg, yield 57%).

[0921] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenol (100 mg) was dissolved in dimethylformamide (2 ml) to prepare a solution. Sodium hydride (16 mg) was then added to the solution, and the mixture was stirred at room temperature for 10 min. A solution of the compound (1) (85 mg) in dimethylformamide was added thereto, and the mixture was further stirred at room temperature for 2 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with ethyl acetate, followed by washing three times with saturated brine. The extract was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (148 mg, yield 98%).

[0922] The resultant compound (145 mg) was dissolved in a 10% hydrochloric acid-methanol solution (5 ml) to prepare a solution which was then allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 106 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.17 (s, 3H), 2.20 - 2.26 (m, 2H), 4.04 (s, 3H), 4.05 (s, 3H), 4.16 (t, J = 6.1 Hz, 2H), 4.24 (t, J = 6.1 Hz, 2H), 6.80 - 6.87 (m, 2H), 6.96 (d, J = 7.8 Hz, 1H), 7.12 - 7.21 (m, 4H), 7.33 - 7.38 (m, 2H), 7.69 (s, 1H), 7.75 (s, 1H), 8.81 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 446 (M⁺+1)

Example 793: 6,7-Dimethoxy-4-{4-[3-(3-methoxyphenoxy)propoxy]phenoxy}quinoline

[0923] 3-Methoxyphenol (300 mg) was dissolved in acetone (5 ml) to prepare a solution. 1,3-Dibromopropane (0.74 ml), potassium carbonate (668 mg), and tetra-n-butylammonium iodide (89 mg) were added to the solution, and the mixture was heated under reflux for 4 hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(3-bromopropyl)-3-methoxybenzene (1) (440 mg, yield 74%).

[0924] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenol (100 mg) was dissolved in dimethylformamide (2 ml) to prepare a solution. Sodium hydride (16 mg) was then added to the solution, and the mixture was stirred at room temperature for 10 min. A solution of the compound (1) (91 mg) in dimethylformamide was added thereto, and the mixture was further stirred at room temperature for 2 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with ethyl acetate, followed by washing three times with saturated brine. The extract was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (147 mg, yield 95%).

[0925] The resultant compound (143 mg) was dissolved in a 10% hydrochloric acid-methanol solution (5 ml) to prepare a solution which was then allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 109 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.17 - 2.24 (m, 2H), 3.73 (s, 3H), 4.03 (s, 3H), 4.04 (s, 3H), 4.15 (t, J = 6.1 Hz,

2H), 4.20 (t, J = 6.1 Hz, 2H), 6.51 - 6.57 (m, 3H), 6.80 (d, J = 6.8 Hz, 1H), 7.15 - 7.21 (m, 3H), 7.32 - 7.37 (m, 2H), 7.64 (s, 1H), 7.74 (s, 1H), 8.77 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 462 (M⁺+1)

5 Example 794: 6,7-Dimethoxy-4-[4-[3-(4-methoxyphenoxy)propoxy]phenoxy]quinoline

[0926] 4-Methoxyphenol (300 mg) was dissolved in acetone (5 ml) to prepare a solution. 1,3-Dibromopropane (0.74 ml), potassium carbonate (668 mg), and tetra-n-butylammonium iodide (89 mg) were then added to the solution, and the mixture was heated under reflux for 7 hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(3-bromopropyl)-4-methoxybenzene (1) (399 mg, yield 67%).

[0927] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenol (100 mg) was dissolved in dimethylformamide (2 ml) to prepare a solution. Sodium hydride (16 mg) was then added to the solution, and the mixture was stirred at room temperature for 10 min. A solution of the compound (1) (91 mg) in dimethylformamide was added thereto, and the mixture was further stirred at room temperature for 6 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with ethyl acetate, followed by washing three times with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (150 mg, yield 97%).

[0928] The resultant compound (141 mg) was dissolved in a 10% hydrochloric acid-methanol solution (5 ml) to prepare a solution which was then allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 135 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.15 - 2.23 (m, 2H), 3.70 (s, 3H), 4.03 (s, 3H), 4.04 (s, 3H), 4.10 (t, J = 6.3 Hz, 2H), 4.20 (t, J = 6.1 Hz, 2H), 6.80 (d, J = 6.6 Hz, 1H), 6.84 - 6.93 (m, 4H), 7.15 - 7.20 (m, 2H), 7.32 - 7.37 (m, 2H), 7.64 (s, 1H), 7.74 (s, 1H), 8.77 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 462 (M⁺+1)

30 Example 795: 6,7-Dimethoxy-4-[4-[3-(2-methoxyphenoxy)propoxy]phenoxy]quinoline

[0929] Guaiacol (300 mg) was dissolved in acetone (5 ml) to prepare a solution. 1,3-Dibromopropane (0.74 ml), potassium carbonate (668 mg), and tetra-n-butylammonium iodide (89 mg) were then added to the solution, and the mixture was heated under reflux for 7 hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(3-bromopropyl)-2-methoxybenzene (1) (449 mg, yield 76%).

[0930] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenol (100 mg) was dissolved in dimethylformamide (2 ml) to prepare a solution. Sodium hydride (16 mg) was then added to the solution, and the mixture was stirred at room temperature for 10 min. A solution of the compound (1) (91 mg) in dimethylformamide was added thereto, and the mixture was further stirred at room temperature for 6 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with ethyl acetate, followed by washing three times with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (116 mg, yield 75%).

[0931] The resultant compound (103 mg) was dissolved in a 10% hydrochloric acid-methanol solution (5 ml) to prepare a solution which was then allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 86 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.17 - 2.24 (m, 2H), 3.76 (s, 3H), 4.03 (s, 3H), 4.04 (s, 3H), 4.14 (t, J = 6.1 Hz, 2H), 4.21 (t, J = 6.1 Hz, 2H), 6.79 (d, J = 6.6 Hz, 1H), 6.86 - 7.03 (m, 4H), 7.15 - 7.20 (m, 2H), 7.32 - 7.37 (m, 2H), 7.66 (s, 1H), 7.74 (s, 1H), 8.76 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 462 (M⁺+1)

55 Example 796: 4-[4-[3-(2-Fluorophenoxy)propoxy]phenoxy]-6,7-dimethoxyquinoline

[0932] o-Fluorophenol (400 mg) was dissolved in acetone (5 ml) to prepare a solution. 1,3-Dibromopropane (1.09 ml), potassium carbonate (985 mg), and tetra-n-butylammonium iodide (132 mg) were then added to the solution, and

the mixture was heated under reflux for 3 hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(3-bromopropyl)-2-fluorobenzene (1) (750 mg, yield 91%).

[0933] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenol (100 mg) was dissolved in dimethylformamide (2 ml) to prepare a solution. Sodium hydride (16 mg) was then added to the solution, and the mixture was stirred at room temperature for 10 min. A solution of the compound (1) (86 mg) in dimethylformamide was added thereto, and the mixture was further stirred at room temperature for 5 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with ethyl acetate, followed by washing three times with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (131 mg, yield 78%).

[0934] The resultant compound (128 mg) was dissolved in a 10% hydrochloric acid-methanol solution (5 ml) to prepare a solution which was then allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 116 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.21 - 2.27 (m, 2H), 4.03 (s, 3H), 4.04 (s, 3H), 4.19 - 4.27 (m, 4H), 6.81 (d, J = 6.6 Hz, 1H), 6.92 - 6.98 (m, 1H), 7.11 - 7.25 (m, 5H), 7.33 - 7.37 (m, 2H), 7.63 - 7.69 (m, 1H), 7.75 (s, 1H), 8.78 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 450 (M⁺+1)

Example 797: 4-{4-[3-(3-Fluorophenoxy)propoxy]phenoxy}-6,7-dimethoxyquinoline

[0935] 3-Fluorophenol (400 mg) was dissolved in acetone (5 ml) to prepare a solution. 1,3-Dibromopropane (1.09 ml), potassium carbonate (985 mg), and tetra-n-butylammonium iodide (132 mg) were then added to the solution, and the mixture was heated under reflux for 3 hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(3-bromopropyl)-3-fluorobenzene (1) (808 mg, yield 97%).

[0936] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenol (100 mg) was dissolved in dimethylformamide (2 ml) to prepare a solution. Sodium hydride (16 mg) was then added to the solution, and the mixture was stirred at room temperature for 10 min. A solution of the compound (1) (86 mg) in dimethylformamide was added thereto, and the mixture was further stirred at room temperature for 5 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with ethyl acetate, followed by washing three times with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (128 mg, yield 84%).

[0937] The resultant compound (123 mg) was dissolved in a 10% hydrochloric acid-methanol solution (5 ml) to prepare a solution which was then allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 109 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.18 - 2.25 (m, 2H), 4.04 (s, 3H), 4.05 (s, 3H), 4.17 - 4.22 (m, 4H), 6.74 - 6.88 (m, 4H), 7.15 - 7.20 (m, 2H), 7.29 - 7.38 (m, 3H), 7.61 - 7.73 (m, 1H), 7.76 (s, 1H), 8.79 (d, J = 6.8 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 450 (M⁺+1)

Example 798: 4-[4-f3-(4-Fluorophenoxy)propoxy]phenoxy]-6,7-dimethoxyquinoline

[0938] 4-Fluorophenol (400 mg) was dissolved in acetone (5 ml) to prepare a solution. 1,3-Dibromopropane (1.09 ml), potassium carbonate (985 mg), and tetra-n-butylammonium iodide (132 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(3-bromopropyl)-4-fluorobenzene (1) (713 mg, yield 86%).

[0939] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenol (100 mg) was dissolved in dimethylformamide (2 ml) to prepare a solution. Sodium hydride (16 mg) was then added to the solution, and the mixture was stirred at room temperature for 10 min. A solution of the compound (1) (86 mg) in dimethylformamide was added thereto, and the mixture was further stirred at room temperature for 4 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with ethyl acetate, followed by washing three times with saturated brine. The

extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (91 mg, yield 60%).

[0940] The resultant compound (85 mg) was dissolved in a 10% hydrochloric acid-methanol solution (5 ml) to prepare a solution which was then allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 90 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.16 - 2.24 (m, 2H), 4.04 (s, 3H), 4.05 (s, 3H), 4.14 (t, J = 6.1 Hz, 2H), 4.20 (t, J = 6.1 Hz, 2H), 6.82 (d, J = 6.6 Hz, 1H), 6.95 - 7.01 (m, 2H), 7.09 - 7.20 (m, 4H), 7.33 - 7.37 (m, 2H), 7.67 (s, 1H), 7.75 (s, 1H), 8.79 (d, J = 6.8 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 450 (M⁺+1)

Example 799: 4-{4-[3-(2,6-Dimethylphenoxy)propoxy]phenoxy}-6,7-dimethoxyquinoline

[0941] 2,6-Dimethylphenol (400 mg) was dissolved in acetone (5 ml) to prepare a solution. 1,3-Dibromopropane (1.00 ml), potassium carbonate (903 mg), and tetra-n-butylammonium iodide (121 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(3-bromopropyl)-2,6-dimethylbenzene (1) (637 mg, yield 81%).

[0942] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenol (100 mg) was dissolved in dimethylformamide (2 ml) to prepare a solution. Sodium hydride (16 mg) was then added to the solution, and the mixture was stirred at room temperature for 10 min. A solution of the compound (1) (90 mg) in dimethylformamide was added thereto, and the mixture was further stirred at room temperature for 4 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with ethyl acetate, followed by washing three times with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (137 mg, yield 88%).

[0943] The resultant compound (116 mg) was dissolved in a 10% hydrochloric acid-methanol solution (5 ml) to prepare a solution which was then allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 75 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.21 (s, 6H), 2.22 (t, J = 6.1 Hz, 2H), 3.92 (t, J = 6.1 Hz, 2H), 4.04 (s, 3H), 4.04 (s, 3H), 4.29 (t, J = 6.1 Hz, 2H), 6.80 (d, J = 6.6 Hz, 1H), 6.89 - 6.94 (m, 1H), 7.01 (s, 1H), 7.03 (s, 1H), 7.17 - 7.22 (m, 2H), 7.34 - 7.39 (m, 2H), 7.70 (s, 1H), 7.75 (s, 1H), 8.80 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 460 (M⁺+1)

Example 800: N1-(3-Methoxyphenyl)-2-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenoxy}acetamide

[0944] 2-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenoxy}acetic acid (150 mg), WSC·HCl (122 mg), and HOBT·H₂O (86 mg) were dissolved in chloroform (5 ml) to prepare a solution. m-Anisidine (63 mg) was then added to the solution, and the mixture was stirred at room temperature for 4 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The chloroform layer was washed with 1 N hydrochloric acid, water, and saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (29 mg, yield 15%).

¹H-NMR (chloroform-d, 400 MHz): δ 3.84 (s, 3H), 4.08 (s, 3H), 4.08 (s, 3H), 4.65 (s, 2H), 6.71 - 6.75 (m, 1H), 7.07 - 7.13 (m, 3H), 7.24 - 7.28 (m, 2H), 7.35 (t, J = 2.2 Hz, 1H), 7.40 (s, 1H), 7.56 (s, 1H), 8.25 (s, 1H), 8.64 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 462 (M⁺+1)

Example 801: N1-(3-Methoxybenzyl)-2-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenoxy}acetamide

[0945] 2-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenoxy}acetic acid (150 mg), WSC·HCl (122 mg), and HOBT·H₂O (86 mg) were dissolved in chloroform (5 ml) to prepare a solution. 3-Methoxybenzylamine (70 mg) was then added to the solution, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The chloroform

layer was washed with 1 N hydrochloric acid, water, and saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (31 mg, yield 16%).

¹H-NMR (chloroform-d, 400 MHz): δ 3.81 (s, 3H), 4.07 (s, 6H), 4.54 (s, 1H), 4.56 (s, 1H), 4.60 (s, 2H), 6.82 - 6.93 (m, 3H), 6.99 - 7.05 (m, 2H), 7.19 - 7.23 (m, 2H), 7.27 - 7.31 (m, 1H), 7.35 (s, 1H), 7.55 (s, 1H), 8.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 476 (M⁺+1)

Example 802: 2-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenoxy}-1-(1,2,3,4-tetrahydro-2-isoquinolyl)-1-ethanone

[0946] 2-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenoxy}acetic acid (100 mg), WSC·HCl (81 mg), and HOBT·H₂O (57 mg) were dissolved in chloroform (3 ml) to prepare a solution. 1,2,3,4-Tetrahydro-isoquinoline (45 mg) was then added to the solution, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (39 mg, yield 30%).

¹H-NMR (chloroform-d, 400 MHz): δ 2.88 - 2.98 (m, 2H), 3.80 - 3.90 (m, 2H), 4.07 (s, 3H), 4.07 (s, 3H), 4.76 (s, 1H), 4.78 (s, 1H), 4.80 (s, 2H), 7.04 - 7.24 (m, 8H), 7.35 (s, 1H), 7.55 (s, 1H), 8.63 (d, J = 3.7 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 472 (M⁺+1)

Example 803: 2-{4-[(6,7-Dimethoxy-4-quinazolinyl)-oxy]phenoxy}-1-(4-phenylpiperidino)-1-ethanone

[0947] 2-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenoxy}acetic acid (100 mg), WSC·HCl (81 mg), and HOBT·H₂O (57 mg) were dissolved in chloroform (3 ml) to prepare a solution. 4-Phenylpiperidine (54 mg) was then added to the solution, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (42 mg, yield 30%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.61 - 1.73 (m, 2H), 1.90 - 2.00 (m, 2H), 2.68 - 2.83 (m, 2H), 3.16 - 3.26 (m, 1H), 4.08 (s, 3H), 4.14 (s, 3H), 4.08 - 4.20 (m, 2H), 4.76 (s, 1H), 4.77 (s, 1H), 7.06 - 7.12 (m, 2H), 7.17 - 7.34 (m, 7H), 7.39 (s, 1H), 7.56 (s, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 500 (M⁺+1)

Example 804: 1-(4-Benzylpiperidino)-2-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenoxy}-1-ethanone

[0948] 2-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenoxy}acetic acid (100 mg), WSC·HCl (81 mg), and HOBT·H₂O (57 mg) were dissolved in chloroform (3 ml) to prepare a solution. 4-Benzylpiperidine (59 mg) was then added to the solution, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (36 mg, yield 25%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.15 - 1.30 (m, 2H), 1.73 (d, J = 13.7 Hz, 2H), 1.76 - 1.88 (m, 1H), 2.53 - 2.66 (m, 3H), 2.98 - 3.09 (m, 1H), 3.94 - 4.02 (m, 1H), 4.09 (s, 3H), 4.12 (s, 3H), 4.54 - 4.62 (m, 1H), 4.71 (s, 2H), 7.03 - 7.10 (m, 2H), 7.12 - 7.24 (m, 5H), 7.25 - 7.33 (m, 2H), 7.58 (s, 1H), 7.63 (s, 1H), 8.69 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 514 (M⁺+1)

Example 805: 2-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenoxy}-1-(4-piperidinopiperidino)-1-ethanone

[0949] 2-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenoxy}acetic acid (100 mg), WSC·HCl (81 mg), and HOBT·H₂O (57 mg) were dissolved in chloroform (3 ml) to prepare a solution. 4-Piperidinopiperidine (57 mg) was then added to the solution, and the mixture was stirred at room temperature overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was

washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (34 mg, yield 24%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.42 - 2.08 (m, 10H), 2.58 - 2.90 (m, 5H), 3.05 - 3.15 (m, 1H), 4.07 (s, 6H), 4.12 - 4.20 (m, 1H), 4.65 - 4.72 (m, 1H), 4.71 (s, 1H), 4.73 (s, 1H), 7.02 - 7.08 (m, 2H), 7.16 - 7.22 (m, 2H), 7.32 (s, 1H), 7.55 (s, 1H), 8.61 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 507 (M⁺+1)

Example 806: 2-[4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenoxy]-1-piperidino-1-ethanone

[0950] 2-[4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenoxy]acetic acid (100 mg), WSC·HCl (81 mg), and HOBT·H₂O (57 mg) were dissolved in chloroform (3 ml) to prepare a solution. Piperidine (29 mg) was then added to the solution, and the mixture was stirred at room temperature for 3 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (31 mg, yield 26%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.54 - 1.90 (m, 6H), 3.49 - 3.61 (m, 4H), 4.07 (s, 3H), 4.08 (s, 3H), 4.71 (s, 2H), 7.04 - 7.09 (m, 2H), 7.16 - 7.20 (m, 2H), 7.40 (s, 1H), 7.56 (s, 1H), 8.64 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 424 (M⁺+1)

Example 807 : N-(2-[4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenoxy]ethyl)-N,N-diethylamine

[0951] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenol (100 mg) was dissolved in dimethylformamide (2 ml) to prepare a solution. Sodium hydride (27 mg) was then added to the solution, and the mixture was stirred at room temperature for 10 min. 2-(Diethylamino)ethyl bromide hydrobromide (88 mg) was added to the solution, and the mixture was stirred at room temperature for 2 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with ethyl acetate. The extract was washed with saturated brine and was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (30 mg, yield 23%).

¹H-NMR (chloroform-d, 400 MHz): δ 1.20 - 1.44 (m, 6H), 2.80 - 3.15 (m, 4H), 3.15 - 3.30 (m, 2H), 4.07 (s, 3H), 4.07 (s, 3H), 4.27 - 4.45 (m, 2H), 6.98 - 7.03 (m, 2H), 7.16 - 7.20 (m, 2H), 7.32 (s, 1H), 7.56 (s, 1H), 8.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 398 (M⁺+1)

Example 808: 4-[4-[3-(4-Fluorophenoxy)propoxy]phenoxy]-6,7-dimethoxyquinazoline

[0952] 4-Fluorophenol (1 g) was dissolved in acetone (10 ml) to prepare a solution. 1,3-Dibromopropane (2.72 ml), potassium carbonate (2.46 g), and tetra-n-butylammonium iodide (329 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(3-bromopropyl)-4-fluorobenzene (1) (1.89 g, yield 91%).

[0953] 4-Hydroxyphenyl benzoate (300 mg) was dissolved in dimethylformamide (2 ml) to prepare a solution. Sodium hydride (84 mg) was then added to the solution, and the mixture was stirred at room temperature for 10 min. A solution of the compound (1) (650 mg) in dimethylformamide was added thereto, and the mixture was further stirred at room temperature for one hr. A saturated aqueous ammonium chloride solution was added to the reaction solution, and the mixture was extracted with ethyl acetate, followed by washing three times with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give 4-[3-(4-fluorophenoxy)propoxy]phenyl benzoate (2) (412 mg, yield 81%).

[0954] The compound (2) (412 mg) was dissolved in methanol (3 ml) to prepare a solution. Sodium hydroxide (60 mg) was added to the solution, and the mixture was stirred at room temperature for 3 hr. A saturated aqueous ammonium chloride solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation

under the reduced pressure, and the residue was purified by chromatography on silica gel using hexane/acetone for development to give 4-[3-(4-fluorophenoxy)propoxy]phenol (3) (229 mg, yield 78%).

[0955] Chlorobenzene (0.4 ml) was added to the compound (3) (225 mg) and 4-chloro-6,7-dimethoxyquinazoline (275 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (117 mg, yield 31%).

¹H-NMR (chloroform-d, 400 MHz): δ 2.24 - 2.31 (m, 2H), 4.07 (s, 6H), 4.14 (t, J = 6.1 Hz, 2H), 4.19 (t, J = 6.1 Hz, 2H), 6.83 - 6.88 (m, 2H), 6.94 - 7.03 (m, 4H), 7.14 - 7.19 (m, 2H), 7.33 (s, 1H), 7.56 (s, 1H), 8.63 (s, 1H)

Mass spectrometry value (FD-MS, m/z) : 450 (M⁺)

Example 809: 6,7-Dimethoxy-4-[4-[3-(3-methoxyphenoxy)propoxy]phenoxy]quinazoline

[0956] 3-Methoxyphenol (1 g) was dissolved in acetone (10 ml) to prepare a solution. 1,3-Dibromopropane (2.45 ml), potassium carbonate (2.22 g), and tetra-n-butylammonium iodide (297 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(3-bromopropyl)-3-methoxybenzene (1) (1.79 g, yield 91%).

[0957] 4-Hydroxyphenyl benzoate (300 mg) was dissolved in dimethylformamide (2 ml) to prepare a solution. Sodium hydride (84 mg) was then added to the solution, and the mixture was stirred at room temperature for 10 min. A solution of the compound (1) (686 mg) in dimethylformamide was added thereto, and the mixture was further stirred at room temperature for one hr. A saturated aqueous ammonium chloride solution was added to the reaction solution, and the mixture was extracted with ethyl acetate, followed by washing three times with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give 4-[3-(3-methoxyphenoxy)propoxy]-phenyl benzoate (2) (252 mg, yield 48%).

[0958] The compound (2) (252 mg) was dissolved in methanol (2 ml) to prepare a solution. Sodium hydroxide (60 mg) was then added to the solution, and the mixture was stirred at room temperature for 3 hr. A saturated aqueous ammonium chloride solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give 4-[3-(3-methoxyphenoxy)propoxy]phenol (3) (146 mg, yield 80%).

[0959] Chlorobenzene (0.4 ml) was added to the compound (3) (143 mg) and 4-chloro-6,7-dimethoxyquinazoline (167 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (118 mg, yield 50%).

¹H-NMR (chloroform-d, 400 MHz): δ 2.24 - 2.32 (m, 2H), 3.80 (s, 3H), 4.07 (s, 6H), 4.15 - 4.22 (m, 4H), 6.48 - 6.55 (m, 3H), 6.98 - 7.03 (m, 2H), 7.14 - 7.21 (m, 3H), 7.35 (s, 1H), 7.56 (s, 1H), 8.63 (s, 1H)

Mass spectrometry value (FD-MS, m/z): 462 (M⁺)

Example 810: 6,7-Dimethoxy-4-[4-[3-(2-methoxyphenoxy)propoxy]phenoxy]quinazoline

[0960] 2-Methoxyphenol (750 mg) was dissolved in acetonitrile (8 ml) to prepare a solution. 1,3-Dibromopropane (0.92 ml) and potassium carbonate (1.25 g) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(3-bromopropyl)-2-methoxybenzene (1).

[0961] 4-Hydroxyphenyl benzoate (650 mg) was dissolved in dimethylformamide (6 ml) to prepare a solution. Sodium hydride (97 mg) was then added to the solution, and the mixture was stirred at room temperature for 10 min. A solution of the compound (1) (1.12 g) in dimethylformamide was added thereto, and the mixture was further stirred at room temperature for one hr. A saturated aqueous ammonium chloride solution was added to the reaction solution, and the mixture was extracted with ethyl acetate, followed by washing three times with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue

was purified by chromatography on silica gel using hexane/acetone for development to give 4-[3-(2-methoxyphenoxy)propoxy]-phenyl benzoate (2) (1.15 g, yield 50%).

[0962] The compound (2) (1.15 g) was dissolved in methanol (10 ml) to prepare a solution. Sodium hydroxide (20 mg) was added to the solution, and the mixture was stirred at room temperature for 3 hr. A saturated aqueous ammonium chloride solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give 4-[3-(2-methoxyphenoxy)propoxy]phenol (3) (0.55 g, yield 66%).

[0963] Chlorobenzene (0.4 ml) was added to the compound (3) (205 mg) and 4-chloro-6,7-dimethoxyquinazoline (252 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (128 mg, yield 37%).

¹H-NMR (chloroform-d, 400 MHz): δ 2.30 - 2.38 (m, 2H), 3.87 (s, 3H), 4.08 (s, 3H), 4.09 (s, 3H), 4.21 - 4.26 (m, 4H), 6.88 - 6.96 (m, 4H), 6.99 - 7.03 (m, 2H), 7.13 - 7.17 (m, 2H), 7.47 (s, 1H), 7.57 (s, 1H), 8.66 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 463 (M⁺+1)

[0964] The resultant compound (125 mg) was dissolved in a 10% hydrochloric acid-methanol solution (6 ml) to prepare a solution which was then allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 61 mg of a hydrochloride.

Example 811: 4-{4-[3-(1H-1-Indolyl)propoxy]phenoxy}-6,7-dimethoxyquinazoline

[0965] Dimethyl sulfoxide (25 ml) was added to potassium hydroxide (2.18 g), and the mixture was stirred. A solution of indole (3 g) in dimethyl sulfoxide was added dropwise thereto, and the mixture was stirred at room temperature for 10 min. 3-Bromo-1-propanol (2.31 ml) was added thereto, and the mixture was stirred at room temperature for 5 hr. Water was added to the reaction solution, and the mixture was extracted with ethyl acetate, followed by washing three times with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give 1-(3-bromopropyl)-1H-indole (1) (3.78 g, yield 84%).

[0966] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenol (100 mg), the compound (1) (59 mg), and triphenylphosphine (106 mg) were dissolved in tetrahydrofuran (3 ml) to prepare a solution. Diethyl azodicarboxylate (0.063 ml) was then added to the solution, and the mixture was stirred at room temperature for 3 hr. The solvent was removed by distillation under the reduced pressure. Water was added to the residue, and the mixture was extracted with ethyl acetate, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using hexane/acetone for development. Diethyl ether was added to the purification product, and the precipitated crystal was collected by filtration and was washed to give the title compound (3 mg, yield 2%).

Mass spectrometry value (FD-MS, m/z) : 455 (M⁺)

Example 812: 6,7-Dimethoxy-4-(4-{[2-(3-methoxyphenoxy)ethyl]sulfanyl}phenoxy)quinoline

[0967] 3-Methoxyphenol (0.6 g) was dissolved in acetone (2 ml) to prepare a solution. 1-Bromo-2-chloroethane (0.60 ml), potassium carbonate (1.00 g), and tetra-n-butylammonium iodide (180 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(2-chloroethoxy)-3-methoxybenzene (1) (348 mg, yield 39%).

[0968] The compound (1) (206 mg) was dissolved in acetone (1 ml) to prepare a solution. 4-Hydroxythiophenol (160 mg) and potassium carbonate (168 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-{[2-(3-methoxyphenoxy)ethyl]sulfanyl}phenol (2) (116 mg, yield 38%).

[0969] Chlorobenzene (0.2 ml) was added to the compound (2) (105 mg) and 4-chloro-6,7-dimethoxyquinoline (170 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was

added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (26 mg, yield 15%).

[0970] The resultant compound (20 mg) was dissolved in a 10% hydrochloric acid-methanol solution (3 ml) to prepare a solution which was then allowed to stand at room temperature for 15 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 17 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.41 (t, J = 6.3 Hz, 2H), 3.72 (s, 3H), 4.01 (s, 3H), 4.03 (s, 3H), 4.19 (t, J = 6.3 Hz, 2H), 6.44 - 6.55 (m, 3H), 6.85 (d, J = 6.6 Hz, 1H), 7.18 (t, J = 8.1 Hz, 1H), 7.36 - 7.41 (m, 2H), 7.60 (s, 1H), 7.61 - 7.65 (m, 2H), 7.72 (s, 1H), 8.77 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 464 (M⁺+1)

Example 813: 6,7-Dimethoxy-4-(4-{[2-(4-methoxyphenoxy)ethyl]sulfanyl}phenoxy)quinoline

[0971] 4-Methoxyphenol (0.6 g) was dissolved in acetone (2 ml) to prepare a solution. 1-Bromo-2-chloroethane (0.60 ml), potassium carbonate (1.00 g), and tetra-n-butylammonium iodide (180 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(2-chloroethoxy)-4-methoxybenzene (1) (246 mg, yield 27%).

[0972] The compound (1) (226 mg) was dissolved in acetone (2 ml) to prepare a solution. 4-Hydroxythiophenol (170 mg) and potassium carbonate (184 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-{[2-(4-methoxyphenoxy)ethyl]sulfanyl}phenol (2) (114 mg, yield 34%).

[0973] Chlorobenzene (0.3 ml) was added to the compound (2) (102 mg) and 4-chloro-6,7-dimethoxyquinoline (165 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (80 mg, yield 47%).

[0974] The resultant compound (66 mg) was dissolved in a 10% hydrochloric acid-methanol solution (6 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 51 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.39 - 3.42 (m, 2H), 3.68 (s, 3H), 4.00 (s, 3H), 4.03 (s, 3H), 4.13 (t, J = 6.1 Hz, 2H), 6.81 - 6.84 (m, 1H), 6.85 (s, 2H), 6.85 (s, 2H), 7.33 - 7.39 (m, 2H), 7.53 (s, 1H), 7.57 - 7.63 (m, 2H), 7.70 (s, 1H), 8.75 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 464 (M⁺+1)

Example 814: 6,7-Dimethoxy-4-(4-{[2-(4-methylphenoxy)ethyl]sulfanyl}phenoxy)quinoline

[0975] p-Cresol (0.6 g) was dissolved in acetone (2 ml) to prepare a solution. 1-Bromo-2-chloroethane (0.69 ml), potassium carbonate (1.15 g), and tetra-n-butylammonium iodide (205 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(2-chloroethoxy)-4-methylbenzene (1) (348 mg, yield 37%).

[0976] The compound (1) (326 mg) was dissolved in acetone (2 ml) to prepare a solution. 4-Hydroxythiophenol (265 mg) and potassium carbonate (290 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-{[2-(4-methylphenoxy)ethyl]sulfanyl}phenol (2) (185 mg, yield 37%).

[0977] Chlorobenzene (0.5 ml) was added to the compound (2) (170 mg) and 4-chloro-6,7-dimethoxyquinoline (292 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was

added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (124 mg, yield 42%).

[0978] The resultant compound (124 mg) was dissolved in a 10% hydrochloric acid-methanol solution (4 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 105 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.21 (s, 3H), 3.39 - 3.42 (m, 2H), 4.01 (s, 3H), 4.03 (s, 3H), 4.15 (t, J = 6.1 Hz, 2H), 6.77 - 6.83 (m, 2H), 6.86 (d, J = 6.6 Hz, 1H), 7.04 - 7.10 (m, 2H), 7.34 - 7.40 (m, 2H), 7.56 (s, 1H), 7.57 - 7.64 (m, 2H), 7.72 (s, 1H), 8.77 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 448 (M⁺+1)

Example 815: 4-(4-{[2-(2-Isopropylphenoxy)ethyl]sulfanyl}phenoxy)-6,7-dimethoxyquinoline

[0979] 2-Isopropylphenol (1 g) was dissolved in acetone (3 ml) to prepare a solution. 1-Bromo-2-chloroethane (0.92 ml), potassium carbonate (1.52 g), and tetra-n-butylammonium iodide (271 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(2-chloroethoxy)-2-isopropylbenzene (1) (480 mg, yield 33%).

[0980] The compound (1) (438 mg) was dissolved in acetone (3 ml) to prepare a solution. 4-Hydroxythiophenol (306 mg) and potassium carbonate (335 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-{[2-(2-isopropylphenoxy)ethyl]sulfanyl}phenol (2) (288 mg, yield 46%).

[0981] Chlorobenzene (0.5 ml) was added to the compound (2) (252 mg) and 4-chloro-6,7-dimethoxyquinoline (390 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (183 mg, yield 44%).

[0982] The resultant compound (123 mg) was dissolved in a 10% hydrochloric acid-methanol solution (4 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 91 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.16 (s, 3H), 1.18 (s, 3H), 3.19 - 3.26 (m, 1H), 3.48 (t, J = 6.1 Hz, 2H), 4.02 (s, 3H), 4.04 (s, 3H), 4.22 (t, J = 6.1 Hz, 2H), 6.85 (d, J = 6.4 Hz, 1H), 6.89 - 6.95 (m, 2H), 7.10 - 7.22 (m, 2H), 7.35 - 7.41 (m, 2H), 7.59 - 7.65 (m, 3H), 7.72 (s, 1H), 8.78 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 476 (M⁺+1)

Example 816: 4-(4-{[2-(4-Isopropylphenoxy)ethyl]sulfanyl}phenoxy)-6,7-dimethoxyquinoline

[0983] 4-Isopropylphenol (1 g) was dissolved in acetone (3 ml) to prepare a solution. 1-Bromo-2-chloroethane (0.92 ml), potassium carbonate (1.52 g), and tetra-n-butylammonium iodide (271 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(2-chloroethoxy)-4-isopropylbenzene (1) (616 mg, yield 42%).

[0984] The compound (1) (590 mg) was dissolved in acetone (4 ml) to prepare a solution. 4-Hydroxythiophenol (412 mg) and potassium carbonate (452 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-{[2-(4-isopropylphenoxy)-ethyl]sulfanyl}phenol (2) (441 mg, yield 52%).

[0985] Chlorobenzene (0.8 ml) was added to the compound (2) (394 mg) and 4-chloro-6,7-dimethoxyquinoline (610 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was

added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (289 mg, yield 44%).

[0986] The resultant compound (217 mg) was dissolved in a 10% hydrochloric acid-methanol solution (4 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 195 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.16 (s, 3H), 1.17 (s, 3H), 2.78 - 2.87 (m, 1H), 3.43 (t, J = 6.3 Hz, 2H), 4.03 (s, 3H), 4.05 (s, 3H), 4.18 (t, J = 6.3 Hz, 2H), 6.82 - 6.87 (m, 2H), 6.89 (d, J = 6.6 Hz, 1H), 7.12 - 7.17 (m, 2H), 7.38 - 7.43 (m, 2H), 7.61 - 7.66 (m, 2H), 7.69 (s, 1H), 7.74 (s, 1H), 8.80 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 476 (M⁺+1)

Example 817: 6,7-Dimethoxy-4-(4-{[2-(2-methylphenoxy)ethyl]sulfanyl}phenoxy)quinoline

[0987] o-Cresol (0.6 g) was dissolved in acetone (2 ml) to prepare a solution. 1-Bromo-2-chloroethane (0.69 ml), potassium carbonate (1.15 g), and tetra-n-butylammonium iodide (205 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(2-chloroethoxy)-2-methylbenzene (1) (345 mg, yield 36%).

[0988] The compound (1) (322 mg) was dissolved in acetone (2 ml) to prepare a solution. 4-Hydroxythiophenol (262 mg) and potassium carbonate (286 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-[[2-(2-methylphenoxy)ethyl]sulfanyl]phenol (2) (231 mg, yield 47%).

[0989] Chlorobenzene (0.3 ml) was added to the compound (2) (204 mg) and 4-chloro-6,7-dimethoxyquinoline (350 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (139 mg, yield 40%).

[0990] The resultant compound (103 mg) was dissolved in a 10% hydrochloric acid-methanol solution (4 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 26 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.13 (s, 3H), 3.47 (t, J = 6.1 Hz, 2H), 4.02 (s, 3H), 4.04 (s, 3H), 4.22 (t, J = 5.9 Hz, 2H), 6.81 - 6.94 (m, 3H), 7.11 - 7.17 (m, 2H), 7.35 - 7.40 (m, 2H), 7.59 (s, 1H), 7.60 - 7.66 (m, 2H), 7.72 (s, 1H), 8.78 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 448 (M⁺+1)

Example 818: 4-(4-{[2-(4-Chlorophenoxy)ethyl]sulfanyl}phenoxy)-6,7-dimethoxyquinoline

[0991] p-Chlorophenol (0.6 g) was dissolved in acetone (2 ml) to prepare a solution. 1-Bromo-2-chloroethane (0.58 ml), potassium carbonate (967 mg), and tetra-n-butylammonium iodide (173 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-chloro-4-(2-chloroethoxy)-benzene (1) (338 mg, yield 38%).

[0992] The compound (1) (338 mg) was dissolved in acetone (3 ml) to prepare a solution. 4-Hydroxythiophenol (246 mg) and potassium carbonate (270 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-[[2-(4-chlorophenoxy)ethyl]sulfanyl]phenol (2) (265 mg, yield 53%).

[0993] Chlorobenzene (0.4 ml) was added to the compound (2) (215 mg) and 4-chloro-6,7-dimethoxyquinoline (343 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was

added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (5 mg, yield 1%).

[0994] The resultant compound (5 mg) was dissolved in a 10% hydrochloric acid-methanol solution (2 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 6 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.44 (t, J = 6.3 Hz, 2H), 4.02 (s, 3H), 4.04 (s, 3H), 4.21 (t, J = 6.1 Hz, 2H), 6.85 (d, J = 6.3 Hz, 1H), 6.93 - 6.99 (m, 2H), 7.30 - 7.35 (m, 2H), 7.38 (s, 1H), 7.40 (s, 1H), 7.60 - 7.65 (m, 3H), 7.72 (s, 1H), 8.78 (d, J = 6.6 Hz, 1H)

Example 819: 4-(4-{[2-(2-Chlorophenoxy)ethyl]sulfanyl}phenoxy)-6,7-dimethoxyquinoline

[0995] 2-Chlorophenol (0.6 g) was dissolved in acetone (2 ml) to prepare a solution. 1-Bromo-2-chloroethane (0.58 ml), potassium carbonate (967 mg), and tetra-n-butylammonium iodide (173 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-chloro-2-(2-chloroethoxy)-benzene (1) (429 mg, yield 48%).

[0996] The compound (1) (412 mg) was dissolved in acetone (4 ml) to prepare a solution. 4-Hydroxythiophenol (300 mg) and potassium carbonate (328 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-{[2-(2-chlorophenoxy)ethyl]sulfanyl}phenol (2) (449 mg, yield 74%).

[0997] Chlorobenzene (0.4 ml) was added to the compound (2) (320 mg) and 4-chloro-6,7-dimethoxyquinoline (510 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (2 mg, yield 0.3%).

[0998] The resultant compound (2 mg) was dissolved in a 10% hydrochloric acid-methanol solution (2 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 2 mg of a hydrochloride.

Mass spectrometry value (ESI-MS, m/z): 468 (M⁺+1)

Example 820: 4-(4-{[2-(3-Chlorophenoxy)ethyl]sulfanyl}phenoxy)-6,7-dimethoxyquinoline

[0999] 3-Chlorophenol (0.6 g) was dissolved in acetone (2 ml) to prepare a solution. 1-Bromo-2-chloroethane (0.58 ml), potassium carbonate (967 mg), and tetra-n-butylammonium iodide (173 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-chloro-3-(2-chloroethoxy)-benzene (1) (400 mg, yield 45%).

[1000] The compound (1) (387 mg) was dissolved in acetone (4 ml) to prepare a solution. 4-Hydroxythiophenol (281 mg) and potassium carbonate (308 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by chromatography on silica gel using chloroform for development to give 4-{[2-(3-chlorophenoxy)ethyl]sulfanyl}phenol (2) (322 mg, yield 57%).

[1001] Chlorobenzene (0.4 ml) was added to the compound (2) (206 mg) and 4-chloro-6,7-dimethoxyquinoline (328 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development

to give the title compound (105 mg, yield 31%).

[1002] The resultant compound (93 mg) was dissolved in a 10% hydrochloric acid-methanol solution (4 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected

by filtration and was washed to give 81 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.43 (t, J = 6.3 Hz, 2H), 4.02 (s, 3H), 4.04 (s, 3H), 4.24 (t, J = 6.1 Hz, 2H), 6.83 - 7.03 (m, 4H), 7.28 - 7.41 (m, 3H), 7.60 - 7.65 (m, 3H), 7.72 (s, 1H), 8.78 (d, J = 6.3 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 468 (M⁺+1)

Example 821: 4-(4-([2-(3-Fluorophenoxy)ethyl]sulfanyl)phenoxy)-6,7-dimethoxyquinoline

[1003] 3-Fluorophenol (0.6 g) was dissolved in acetone (2 ml) to prepare a solution. 1-Bromo-2-chloroethane (0.67 ml), potassium carbonate (1.11 g), and tetra-n-butylammonium iodide (198 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(2-chloroethoxy)-3-fluorobenzene (1) (407 mg, yield 44%).

[1004] The compound (1) (395 mg) was dissolved in acetone (4 ml) to prepare a solution. 4-Hydroxythiophenol (314 mg) and potassium carbonate (344 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by chromatography on silica gel using chloroform for development to give 4-([2-(3-fluorophenoxy)ethyl]sulfanyl)phenol (2) (323 mg, yield 54%).

[1005] Chlorobenzene (0.4 ml) was added to the compound (2) (230 mg) and 4-chloro-6,7-dimethoxyquinoline (390 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (137 mg, yield 35%).

[1006] The resultant compound (110 mg) was dissolved in a 10% hydrochloric acid-methanol solution (4 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 93 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.44 (t, J = 6.3 Hz, 2H), 4.03 (s, 3H), 4.04 (s, 3H), 4.23 (t, J = 6.1 Hz, 2H), 6.74 - 6.84 (m, 3H), 6.86 (d, J = 6.6 Hz, 1H), 7.27 - 7.41 (m, 3H), 7.61 - 7.66 (m, 3H), 7.73 (s, 1H), 8.78 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 452 (M⁺+1)

Example 822: 4-(4-([2-(2-Fluorophenoxy)ethyl]sulfanyl)phenoxy)-6,7-dimethoxyquinoline

[1007] o-Fluorophenol (0.6 g) was dissolved in acetone (2 ml) to prepare a solution. 1-Bromo-2-chloroethane (0.67 ml), potassium carbonate (1.11 g), and tetra-n-butylammonium iodide (198 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(2-chloroethoxy)-2-fluorobenzene (1) (406 mg, yield 44%).

[1008] The compound (1) (387 mg) was dissolved in acetone (2 ml) to prepare a solution. 4-Hydroxythiophenol (308 mg) and potassium carbonate (338 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-([2-(2-fluorophenoxy)ethyl]sulfanyl)phenol (2) (244 mg, yield 42%).

[1009] Chlorobenzene (0.4 ml) was added to the compound (2) (191 mg) and 4-chloro-6,7-dimethoxyquinoline (324 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (132 mg, yield 40%).

[1010] The resultant compound (106 mg) was dissolved in a 10% hydrochloric acid-methanol solution (3 ml) to pre-

pare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 105 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.48 (t, J = 6.6 Hz, 2H), 4.04 (s, 3H), 4.05 (s, 3H), 4.29 (t, J = 6.3 Hz, 2H), 6.89 (d, J = 6.6 Hz, 1H), 6.93 - 7.00 (m, 1H), 7.09 - 7.25 (m, 3H), 7.37 - 7.43 (m, 2H), 7.62 - 7.69 (m, 3H), 7.75 (s, 1H), 8.82 (d, J = 6.8 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 452 (M⁺+1)

Example 823: 6,7-Dimethoxy-4-(4-[[2-(3-methylphenoxy)ethyl]sulfanyl]phenoxy)quinoline

[1011] m-Cresol (0.6 g) was dissolved in acetone (3 ml) to prepare a solution. 1-Bromo-2-chloroethane (0.69 ml), potassium carbonate (1.15 g), and tetra-n-butylammonium iodide (205 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(2-chloroethoxy)-3-methylbenzene (1) (349 mg, yield 37%).

[1012] The compound (1) (337 mg) was dissolved in acetone (3 ml) to prepare a solution. 4-Hydroxythiophenol (275 mg) and potassium carbonate (301 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-[[2-(3-methylphenoxy)ethyl]sulfanyl]phenol (2) (188 mg, yield 36%).

[1013] Chlorobenzene (0.3 ml) was added to the compound (2) (160 mg) and 4-chloro-6,7-dimethoxyquinoline (276 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate, and the solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (129 mg, yield 47%).

[1014] The resultant compound (102 mg) was dissolved in a 10% hydrochloric acid-methanol solution (3 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 68 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.27 (s, 3H), 3.43 (t, J = 6.3 Hz, 2H), 4.02 (s, 3H), 4.04 (s, 3H), 4.19 (t, J = 6.3 Hz, 2H), 6.69 - 6.78 (m, 3H), 6.84 - 6.88 (m, 1H), 7.16 (t, J = 7.8 Hz, 1H), 7.36 - 7.41 (m, 2H), 7.59 - 7.65 (m, 3H), 7.72 (s, 1H), 8.78 (d, J = 6.3 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 448 (M⁺+1)

Example 824: 4-(4-[[2-(4-Fluorophenoxy)ethyl]sulfanyl]phenoxy)-6,7-dimethoxyquinoline

[1015] 4-Fluorophenol (0.6 g) was dissolved in acetone (3 ml) to prepare a solution. 1-Bromo-2-chloroethane (0.69 ml), potassium carbonate (1.11 g), and tetra-n-butylammonium iodide (198 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(2-chloroethoxy)-4-fluorobenzene (1) (352 mg, yield 38%).

[1016] The compound (1) (342 mg) was dissolved in acetone (4 ml) to prepare a solution. 4-Hydroxythiophenol (273 mg) and potassium carbonate (299 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-[[2-(4-fluorophenoxy)ethyl]sulfanyl]phenol (2) (233 mg, yield 45%).

[1017] Chlorobenzene (0.4 ml) was added to the compound (2) (211 mg) and 4-chloro-6,7-dimethoxyquinoline (357 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (181 mg, yield 50%).

[1018] The resultant compound (106 mg) was dissolved in a 10% hydrochloric acid-methanol solution (3 ml) to pre-

pare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 101 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.43 (t, J = 6.6 Hz, 2H), 4.03 (s, 3H), 4.05 (s, 3H), 4.19 (t, J = 6.1 Hz, 2H), 6.88 (d, J = 6.8 Hz, 1H), 6.92 - 6.97 (m, 2H), 7.08 - 7.14 (m, 2H), 7.37 - 7.42 (m, 2H), 7.60 - 7.68 (m, 3H), 7.74 (s, 1H), 8.81 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 452 (M⁺+1)

Example 825: 4-(4-[[2-(2,4-Dichlorophenoxy)ethyl]sulfanyl]phenoxy)-6,7-dimethoxyquinoline

[1019] 2,4-Dichlorophenol (0.6 g) was dissolved in acetone (3 ml) to prepare a solution. 1-Bromo-2-chloroethane (0.46 ml), potassium carbonate (763 mg), and tetra-n-butylammonium iodide (136 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 2,4-dichloro-1-(2-chloroethoxy)benzene (1) (475 mg, yield 57%).

[1020] The compound (1) (462 mg) was dissolved in acetone (4 ml) to prepare a solution. 4-Hydroxythiophenol (285 mg) and potassium carbonate (312 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-[[2-(2,4-dichlorophenoxy)ethyl]sulfanyl]phenol (2) (342 mg, yield 53%).

[1021] Chlorobenzene (0.3 ml) was added to the compound (2) (230 mg) and 4-chloro-6,7-dimethoxyquinoline (326 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (185 mg, yield 51%).

[1022] The resultant compound (103 mg) was dissolved in a 10% hydrochloric acid-methanol solution (10 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 83 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz) : δ 3.48 (t, J = 6.8 Hz, 2H), 4.03 (s, 3H), 4.05 (s, 3H), 4.31 (t, J = 6.1 Hz, 2H), 6.85 - 6.90 (m, 1H), 7.17 - 7.22 (m, 1H), 7.34 - 7.42 (m, 3H), 7.56 - 7.67 (m, 4H), 7.74 (s, 1H), 8.78 - 8.83 (m, 1H)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

Example 826: 4-(4-[[2-(2,4-Dimethylphenoxy)ethyl]sulfanyl]phenoxy)-6,7-dimethoxyquinoline

[1023] 2,4-Dimethylphenol (0.6 g) was dissolved in acetone (3 ml) to prepare a solution. 1-Bromo-2-chloroethane (0.61 ml), potassium carbonate (1.02 g), and tetra-n-butylammonium iodide (183 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(2-chloroethoxy)-2,4-dimethylbenzene (1) (231 mg, yield 26%).

[1024] The compound (1) (224 mg) was dissolved in acetone (2 ml) to prepare a solution. 4-Hydroxythiophenol (168 mg) and potassium carbonate (184 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-[[2-(2,4-dimethylphenoxy)ethyl]sulfanyl]phenol (2) (124 mg, yield 38%).

[1025] Chlorobenzene (0.3 ml) was added to the compound (2) (112 mg) and 4-chloro-6,7-dimethoxyquinoline (182 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (68 mg, yield 36%).

[1026] The resultant compound (51 mg) was dissolved in a 10% hydrochloric acid-methanol solution (3 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 35 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.08 (s, 3H), 2.18 (s, 3H), 3.40 - 3.45 (m, 2H), 4.01 (s, 3H), 4.03 (s, 3H), 4.16 (t, J = 6.1 Hz, 2H), 6.75 - 6.95 (m, 4H), 7.33 - 7.40 (m, 2H), 7.56 (s, 1H), 7.57 - 7.64 (m, 2H), 7.71 (s, 1H), 8.77 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 462 (M⁺+1)

Example 827: 4-(4-[[2-(3,4-Dimethylphenoxy)ethyl]sulfanyl]phenoxy)-6,7-dimethoxyquinoline

[1027] 3,4-Dimethylphenol (0.6 g) was dissolved in acetone (3 ml) to prepare a solution. 1-Bromo-2-chloroethane (0.61 ml), potassium carbonate (1.02 g), and tetra-n-butylammonium iodide (183 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(2-chloroethoxy)-3,4-dimethylbenzene (1) (286 mg, yield 32%).

[1028] The compound (1) (279 mg) was dissolved in acetone (2 ml) to prepare a solution. 4-Hydroxythiophenol (210 mg) and potassium carbonate (230 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-[[2-(3,4-dimethylphenoxy)ethyl]sulfanyl]phenol (2) (190 mg, yield 46%).

[1029] Chlorobenzene (0.3 ml) was added to the compound (2) (138 mg) and 4-chloro-6,7-dimethoxyquinoline (226 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (122 mg, yield 52%).

[1030] The resultant compound (68 mg) was dissolved in a 10% hydrochloric acid-methanol solution (3 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 34 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.13 (s, 3H), 2.18 (s, 3H), 3.40 (t, J = 6.3 Hz, 2H), 4.02 (s, 3H), 4.04 (s, 3H), 4.15 (t, J = 6.3 Hz, 2H), 6.61 - 6.74 (m, 2H), 6.87 (d, J = 6.6 Hz, 1H), 7.02 (d, J = 8.1 Hz, 1H), 7.38 (d, J = 8.8 Hz, 2H), 7.54 - 7.66 (m, 3H), 7.72 (s, 1H), 8.78 (d, J = 6.3 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 462 (M⁺+1)

Example 828: 4-(4-[[2-(2,6-Dimethylphenoxy)ethyl]sulfanyl]phenoxy)-6,7-dimethoxyquinoline

[1031] 2,6-Dimethylphenol (1 g) was dissolved in acetone (4 ml) to prepare a solution. 1-Bromo-2-chloroethane (1.02 ml), potassium carbonate (1.70 g), and tetra-n-butylammonium iodide (303 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(2-chloroethoxy)-2,6-dimethylbenzene (1) (513 mg, yield 34%).

[1032] The compound (1) (513 mg) was dissolved in acetone (4 ml) to prepare a solution. 4-Hydroxythiophenol (386 mg) and potassium carbonate (423 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-[[2-(2,6-dimethylphenoxy)ethyl]sulfanyl]phenol (2) (319 mg, yield 42%).

[1033] Chlorobenzene (0.5 ml) was added to the compound (2) (281 mg) and 4-chloro-6,7-dimethoxyquinoline (456 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the

reduced pressure, and the residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (29 mg, yield 6%).

[1034] The resultant compound (29 mg) was dissolved in a 10% hydrochloric acid-methanol solution (3 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 25 mg of a hydrochloride.

¹H-NMR (chloroform-d, 400 MHz): δ 2.29 (s, 3H), 2.34 (s, 3H), 3.41 (s, 1H), 3.95 - 4.30 (m, 9H), 6.85 - 8.30 (m, 11H)
Mass spectrometry value (ESI-MS, m/z): 462 (M⁺+1)

Example 829: 4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl [2-(4-fluorophenoxy)ethyl]sulfone

[1035] 4-(4-[[2-(4-Fluorophenoxy)ethyl]sulfanyl]phenoxy)-6,7-dimethoxyquinoline (20 mg) was dissolved in acetic acid (0.5 ml) to prepare a solution. Potassium permanganate (35 mg) was added to the solution, and the mixture was stirred at room temperature for 2 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development to give the title compound (16 mg, yield 76%).

[1036] The resultant compound (16 mg) was dissolved in a 10% hydrochloric acid-methanol solution (2 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 17 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.91 (t, J = 5.6 Hz, 2H), 3.99 (s, 3H), 4.03 (s, 3H), 4.30 (t, J = 5.4 Hz, 2H), 6.74 - 6.81 (m, 2H), 6.92 (d, J = 6.3 Hz, 1H), 7.04 - 7.13 (m, 2H), 7.57 (s, 1H), 7.59 - 7.66 (m, 2H), 7.68 (s, 1H), 8.06 - 8.13 (m, 2H), 8.81 (d, J = 6.3 Hz, 1H)
Mass spectrometry value (ESI-MS, m/z): 484 (M⁺+1)

Example 830: 4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl [2-(3-methoxyphenoxy)ethyl]sulfone

[1037] 6,7-Dimethoxy-4-(4-[[2-(3-methoxyphenoxy)ethyl]sulfanyl]phenoxy)quinoline (20 mg) was dissolved in acetic acid (0.5 ml) to prepare a solution. Potassium permanganate (34 mg) was added to the solution, and the mixture was stirred at room temperature for 2 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development to give the title compound (9 mg, yield 40%).

[1038] The resultant compound (9 mg) was dissolved in a 10% hydrochloric acid-methanol solution (2 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 9 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.70 (s, 3H), 3.91 (t, J = 5.6 Hz, 2H), 4.01 (s, 3H), 4.04 (s, 3H), 4.31 (t, J = 5.6 Hz, 2H), 6.23 (t, J = 2.4 Hz, 1H), 6.32 - 6.37 (m, 1H), 6.50 - 6.55 (m, 1H), 6.93 (d, J = 6.1 Hz, 1H), 7.16 (t, J = 8.3 Hz, 1H), 7.57 - 7.69 (m, 4H), 8.07 - 8.13 (m, 2H), 8.80 (d, J = 6.1 Hz, 1H)
Mass spectrometry value (ESI-MS, m/z): 496 (M⁺+1)

Example 831: 2-(2,4-Dichlorophenoxy)ethyl{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}sulfone

[1039] 4-(4-[[2-(2,4-Dichlorophenoxy)ethyl]sulfanyl]phenoxy)-6,7-dimethoxyquinoline (20 mg) was dissolved in acetic acid (0.5 ml) to prepare a solution. Potassium permanganate (32 mg) was added to the solution, and the mixture was stirred at room temperature for 2 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development to give the title compound (15 mg, yield 69%).

[1040] The resultant compound (15 mg) was dissolved in a 10% hydrochloric acid-methanol solution (2 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 15 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.94 - 4.07 (m, 8H), 4.42 (t, J = 5.4 Hz, 2H), 6.91 (d, J = 6.3 Hz, 1H), 7.19 (d, J = 9.0 Hz, 1H), 7.33 - 7.37 (m, 1H), 7.52 - 7.67 (m, 5H), 7.97 - 8.03 (m, 2H), 8.80 (d, J = 6.3 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 533 (M⁺⁺1)

5 Example 832: 2-(3-Chlorophenoxy)ethyl[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]sulfone

[1041] 4-(4-[[2-(3-Chlorophenoxy)ethyl]sulfanyl]phenoxy)-6,7-dimethoxyquinoline (20 mg) was dissolved in acetic acid (0.5 ml) to prepare a solution. Potassium permanganate (31 mg) was added to the solution, and the mixture was stirred at room temperature for 2 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development to give the title compound (10 mg, yield 50%).

[1042] The resultant compound (10 mg) was dissolved in a 10% hydrochloric acid-methanol solution (4 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 10 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.92 (t, J = 5.4 Hz, 2H), 3.99 (s, 3H), 4.03 (s, 3H), 4.35 (t, J = 5.6 Hz, 2H), 6.70 - 6.76 (m, 1H), 6.78 (t, J = 2.0 Hz, 1H), 6.94 (d, J = 6.3 Hz, 1H), 6.97 - 7.03 (m, 1H), 7.28 (t, J = 8.3 Hz, 1H), 7.58 (s, 1H), 7.60 - 7.67 (m, 2H), 7.68 (s, 1H), 8.06 - 8.13 (m, 2H), 8.81 (d, J = 6.3 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 500 (M⁺⁺1)

Example 833: 4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl [2-(3,4-dimethylphenoxy)ethyl]sulfone

[1043] 4-(4-[[2-(3,4-Dimethylphenoxy)ethyl]sulfanyl]phenoxy)-6,7-dimethoxyquinoline (19 mg) was dissolved in acetic acid (0.5 ml) to prepare a solution. Potassium permanganate (33 mg) was added to the solution, and the mixture was stirred at room temperature for 2 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development to give the title compound (4 mg, yield 17%).

[1044] The resultant compound (4 mg) was dissolved in a 10% hydrochloric acid-methanol solution (2 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 4 mg of a hydrochloride.

Mass spectrometry value (ESI-MS, m/z): 494 (M⁺⁺1)

Example 834: 4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl [2-(4-methylphenoxy)ethyl]sulfone

[1045] 6,7-Dimethoxy-4-(4-[[2-(4-methylphenoxy)ethyl]sulfanyl]phenoxy)quinoline (20 mg) was dissolved in acetic acid (0.5 ml) to prepare a solution. Potassium permanganate (32 mg) was added to the solution, and the mixture was stirred at room temperature for 3 hr. Thereafter, water was further added thereto, and the mixture was stirred at room temperature for 5 min. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development to give the title compound (1 mg, yield 4%).

[1046] The resultant compound (1 mg) was dissolved in a 10% hydrochloric acid-methanol solution (2 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 1 mg of a hydrochloride.

Mass spectrometry value (ESI-MS, m/z): 480 (M⁺⁺1)

Example 835: 4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl [2-(4-isopropylphenoxy)ethyl]sulfone

[1047] 4-(4-[[2-(4-Isopropylphenoxy)ethyl]sulfanyl]phenoxy)-6,7-dimethoxyquinoline (22 mg) was dissolved in acetic acid (0.5 ml) to prepare a solution. Potassium permanganate (34 mg) was added to the solution, and the mixture was stirred at room temperature for 3 hr. Thereafter, water was further added thereto, and the mixture was stirred at room

temperature for 10 min. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development to give the title compound (2 mg, yield 8%).

[1048] The resultant compound (2 mg) was dissolved in a 10% hydrochloric acid-methanol solution (2 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 2 mg of a hydrochloride.

Mass spectrometry value (ESI-MS, m/z): 508 ($M^{+}+1$)

Example 836: 4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl [2-(2-isopropylphenoxy)ethyl]sulfone

[1049] 4-(4-[[2-(2-Isopropylphenoxy)ethyl]sulfanyl]phenoxy)-6,7-dimethoxyquinoline (12 mg) was dissolved in acetic acid (0.5 ml) to prepare a solution. Potassium permanganate (19 mg) was added to the solution, and the mixture was stirred at room temperature for 2 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development to give the title compound (7 mg, yield 57%).

[1050] The resultant compound (7 mg) was dissolved in a 10% hydrochloric acid-methanol solution (4 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 7 mg of a hydrochloride.

$^1\text{H-NMR}$ ($\text{DMSO-}d_6$, 400 MHz): δ 1.04 (s, 3H), 1.06 (s, 3H), 2.70 - 2.80 (m, 1H), 3.91 - 4.06 (m, 8H), 4.32 (t, J = 5.4 Hz, 2H), 6.87 - 6.98 (m, 3H), 7.09 - 7.18 (m, 2H), 7.54 - 7.66 (m, 4H), 8.09 - 8.17 (m, 2H), 8.78 (d, J = 6.1 Hz, 1H)
Mass spectrometry value (ESI-MS, m/z): 508 ($M^{+}+1$)

Example 837: 4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl [2-(2-fluorophenoxy)ethyl]sulfone

[1051] 4-(4-[[2-(2-Fluorophenoxy)ethyl]sulfanyl]-phenoxy)-6,7-dimethoxyquinoline (20 mg) was dissolved in acetic acid (0.5 ml) to prepare a solution. Potassium permanganate (33 mg) was added to the solution, and the mixture was stirred at room temperature for 2 hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/acetone for development to give the title compound (7 mg, yield 37%).

[1052] The resultant compound (7 mg) was dissolved in a 10% hydrochloric acid-methanol solution (4 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 7 mg of a hydrochloride.

$^1\text{H-NMR}$ ($\text{DMSO-}d_6$, 400 MHz): δ 3.93 - 4.04 (m, 8H), 4.41 (t, J = 5.4 Hz, 2H), 6.87 - 7.23 (m, 5H), 7.56 - 7.64 (m, 3H), 7.67 (s, 1H), 8.11 (d, J = 8.5 Hz, 2H), 8.84 (d, J = 6.1 Hz, 1H)
Mass spectrometry value (ESI-MS, m/z): 484 ($M^{+}+1$)

Example 838: {4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}[2-(3-methoxy-4-nitrophenoxy)ethyl] sulfoxide

[1053] Nitric acid (0.5 ml) was added to 6,7-dimethoxy-4-(4-[[2-(3-methoxyphenoxy)ethyl]sulfanyl]phenoxy)quinoline (20 mg), and the mixture was stirred at 0°C for 30 min. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (14 mg, yield 60%).

[1054] The resultant compound (14 mg) was dissolved in a 10% hydrochloric acid-methanol solution (2 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 15 mg of a hydrochloride.

Mass spectrometry value (ESI-MS, m/z): 541 ($M^{+}+1$)

Example 839: {4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}[2-(4-fluoro-2-nitrophenoxy)ethyl]sulfoxide

[1055] Nitric acid (0.5 ml) was added to 4-(4-[[2-(4-Fluorophenoxy)ethyl]sulfanyl]phenoxy)-6,7-dimethoxyquinoline (20 mg), and the mixture was stirred at 0°C for 30 min. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (13 mg, yield 58%).

[1056] The resultant compound (13 mg) was dissolved in a 10% hydrochloric acid-methanol solution (2 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 14 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.50 - 3.58 (m, 2H), 4.03 (s, 3H), 4.05 (s, 3H), 4.53 (t, J = 4.9 Hz, 2H), 6.93 - 6.97 (m, 1H), 7.47 - 7.65 (m, 5H), 7.73 (s, 1H), 7.87 - 7.94 (m, 3H), 8.80 (d, J = 6.3 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 513 (M⁺+1)

Example 840: [2-(2,4-Dichlorophenoxy)ethyl]{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl} sulfoxide

[1057] Nitric acid (0.5 ml) was added to 4-(4-[[2-(2,4-dichlorophenoxy)ethyl]sulfanyl]phenoxy)-6,7-dimethoxyquinoline (20 mg), and the mixture was stirred at 0°C for one hr. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by thin-layer chromatography using chloroform/methanol for development to give the title compound (19 mg, yield 92%).

[1058] The resultant compound (19 mg) was dissolved in a 10% hydrochloric acid-methanol solution (2 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 19 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.50 - 3.62 (m, 2H), 4.02 (s, 3H), 4.05 (s, 3H), 4.39 - 4.49 (m, 2H), 6.91 (d, J = 6.3 Hz, 1H), 7.26 (d, J = 9.0 Hz, 1H), 7.37 - 7.43 (m, 1H), 7.57 - 7.64 (m, 4H), 7.72 (s, 1H), 7.90 - 7.97 (m, 2H), 8.81 (d, J = 6.3 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 518 (M⁺+1)

Example 841: 6,7-Dimethoxy-4-(4-[[3-(3-methylphenoxy)propyl]sulfanyl]phenoxy)quinoline

[1059] m-Cresol (0.6 g) was dissolved in acetonitrile (2 ml) to prepare a solution. 1,3-Dibromopropane (1.13 ml), potassium carbonate (2.30 g), and tetra-n-butylammonium iodide (205 mg) were then added to the solution, and the mixture was heated under reflux for 3 hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(3-bromopropoxy)-3-methylbenzene (1) (831 mg, yield 65%).

[1060] The compound (1) (1.07 g) was dissolved in acetone (5 ml) to prepare a solution. 4-Hydroxythiophenol (647 mg) and potassium carbonate (709 mg) were then added to the solution, and the mixture was stirred at room temperature for 2 hr. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-[[3-(3-methylphenoxy)propyl]sulfanyl]phenol (2) (1.00 g, yield 78%).

[1061] Chlorobenzene (0.4 ml) was added to the compound (2) (200 mg) and 4-chloro-6,7-dimethoxyquinoline (326 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (134 mg, yield 37%).

[1062] The resultant compound (110 mg) was dissolved in a 10% hydrochloric acid-methanol solution (4 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 103 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.05 (t, J = 6.8 Hz, 2H), 2.27 (s, 3H), 3.19 (t, J = 7.3 Hz, 2H), 4.04 (s, 3H), 4.05

(s, 3H), 4.08 (t, J = 6.1 Hz, 2H), 6.70 - 6.77 (m, 3H), 6.88 (d, J = 6.6 Hz, 1H), 7.16 (t, J = 8.3 Hz, 1H), 7.37 - 7.42 (m, 2H), 7.55 - 7.61 (m, 2H), 7.69 (s, 1H), 7.75 (s, 1H), 8.80 (d, J = 6.6 Hz, 1H)

Example 842: 4-(4-{[3-(2-Fluorophenoxy)propyl]sulfanyl}phenoxy)-6,7-dimethoxyquinoline

[1063] o-Fluorophenol (0.6 g) was dissolved in acetonitrile (2 ml) to prepare a solution. 1,3-Dibromopropane (1.09 ml), potassium carbonate (2.22 g), and tetra-n-butylammonium iodide (198 mg) were then added to the solution, and the mixture was heated under reflux for one hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(3-bromopropoxy)-3-methylbenzene (1) (930 mg, yield 75%).

[1064] The compound (1) (1.10 g) was dissolved in acetone (5 ml) to prepare a solution. 4-Hydroxythiophenol (657 mg) and potassium carbonate (720 mg) were then added to the solution, and the mixture was stirred at room temperature for 2 hr. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-{[3-(2-fluorophenoxy)propyl]sulfanyl}phenol (2) (853 mg, yield 65%).

[1065] Chlorobenzene (0.4 ml) was added to the compound (2) (200 mg) and 4-chloro-6,7-dimethoxyquinoline (322 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (167 mg, yield 50%).

[1066] The resultant compound (139 mg) was dissolved in a 10% hydrochloric acid-methanol solution (8 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 132 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.04 - 2.13 (m, 2H), 3.20 (t, J = 7.1 Hz, 2H), 4.04 (s, 3H), 4.05 (s, 3H), 4.18 (t, J = 6.1 Hz, 2H), 6.87 (d, J = 6.6 Hz, 1H), 6.91 - 6.98 (m, 1H), 7.10 - 7.24 (m, 3H), 7.36 - 7.42 (m, 2H), 7.59 - 7.63 (m, 2H), 7.69 (s, 1H), 7.74 (s, 1H), 8.80 (d, J = 6.6 Hz, 1H)

Example 843: 4-(4-{[4-(2-Fluorophenoxy)butyl]sulfanyl}phenoxy)-6,7-dimethoxyquinoline

[1067] o-Fluorophenol (1.0 g) was dissolved in acetonitrile (3 ml) to prepare a solution. 1,4-Dibromobutane (2.13 ml), potassium carbonate (3.70 g), and tetra-n-butylammonium iodide (330 mg) were then added to the solution, and the mixture was heated under reflux for one hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(4-bromobutoxy)-2-fluorobenzene (1) (1.57 g, yield 71%).

[1068] The compound (1) (1.55 g) was dissolved in acetone (4 ml) to prepare a solution. 4-Hydroxythiophenol (873 mg) and potassium carbonate (956 mg) were then added to the solution, and the mixture was stirred at room temperature for 2 hr. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-{[4-(2-fluorophenoxy)butyl]sulfanyl}phenol (2) (1.66 g, yield 90%).

[1069] Chlorobenzene (0.4 ml) was added to the compound (2) (200 mg) and 4-chloro-6,7-dimethoxyquinoline (306 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (156 mg, yield 47%).

[1070] The resultant compound (99 mg) was dissolved in a 10% hydrochloric acid-methanol solution (4 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 69 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.73 - 1.95 (m, 4H), 3.12 (t, J = 7.3 Hz, 2H), 4.03 (s, 3H), 4.04 (s, 3H), 4.09 (t, J = 6.1 Hz, 2H), 6.86 (d, J = 6.6 Hz, 1H), 6.88 - 6.97 (m, 1H), 7.08 - 7.23 (m, 3H), 7.34 - 7.39 (m, 2H), 7.52 - 7.57 (m, 2H), 7.61 (s, 1H), 7.73 (s, 1H), 8.78 (d, J = 6.3 Hz, 1H)

Example 844: 6,7-Dimethoxy-4-(4-[[4-(3-methylphenoxy)butyl]sulfanyl]phenoxy)quinoline

[1071] m-Cresol (1 g) was dissolved in acetonitrile (3 ml) to prepare a solution. 1,4-Dibromobutane (2.21 ml), potassium carbonate (3.84 g), and tetra-n-butylammonium iodide (342 mg) were then added to the solution, and the mixture was heated under reflux for one hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(4-bromobutoxy)-3-methylbenzene (1).

[1072] The compound (1) was dissolved in acetone (4 ml) to prepare a solution. 4-Hydroxythiophenol (2.07 g) and potassium carbonate (2.27 g) were then added to the solution, and the mixture was stirred at room temperature for 6 hr. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-[[4-(3-methylphenoxy)butyl]sulfanyl]phenol (2) (1.04 g, yield 39%).

[1073] Chlorobenzene (0.4 ml) was added to the compound (2) (200 mg) and 4-chloro-6,7-dimethoxyquinoline (309 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (139 mg, yield 42%).

[1074] The resultant compound (115 mg) was dissolved in a 10% hydrochloric acid-methanol solution (6 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 85 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.72 - 1.91 (m, 4H), 2.26 (s, 3H), 3.11 (t, J = 7.1 Hz, 2H), 3.98 (t, J = 6.3 Hz, 2H), 4.03 (s, 3H), 4.04 (s, 3H), 6.68 - 6.76 (m, 3H), 6.86 (d, J = 6.6 Hz, 1H), 7.11 - 7.17 (m, 1H), 7.33 - 7.39 (m, 2H), 7.52 - 7.57 (m, 2H), 7.60 (s, 1H), 7.73 (s, 1H), 8.78 (d, J = 6.6 Hz, 1H)

Example 845: 4-(4-[[3-(2-Fluorophenoxy)propyl]sulfanyl]phenoxy)-6,7-dimethoxyquinazoline

[1075] o-Fluorophenol (0.6 g) was dissolved in acetonitrile (2 ml) to prepare a solution. 1,3-Dibromopropane (1.09 ml), potassium carbonate (2.22 g), and tetra-n-butylammonium iodide (198 mg) were then added to the solution, and the mixture was heated under reflux for one hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(3-bromopropoxy)-2-fluorobenzene (1) (930 mg, yield 75%).

[1076] The compound (1) (1.10 g) was dissolved in acetone (5 ml) to prepare a solution. 4-Hydroxythiophenol (657 mg) and potassium carbonate (720 mg) were then added to the solution, and the mixture was stirred at room temperature for 2 hr. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-[[3-(2-fluorophenoxy)propyl]sulfanyl]phenol (2) (0.85 g, yield 65%).

[1077] Chlorobenzene (0.3 ml) was added to the compound (2) (100 mg) and 4-chloro-6,7-dimethoxyquinazoline (163 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (65 mg, yield 39%).

[1078] The resultant compound (60 mg) was dissolved in a 10% hydrochloric acid-methanol solution (8 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 36 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.01 - 2.10 (m, 2H), 3.16 (t, J = 7.3 Hz, 2H), 3.99 (s, 3H), 4.00 (s, 3H), 4.13 - 4.23 (m, 2H), 6.90 - 6.93 (m, 1H), 7.09 - 7.51 (m, 8H), 7.58 (s, 1H), 8.65 (s, 1H)

Example 846: 6,7-Dimethoxy-4-(4-[[3-(3-methylphenoxy)propyl]sulfanyl]phenoxy)quinazoline

[1079] m-Cresol (0.6 g) was dissolved in acetonitrile (2 ml) to prepare a solution. 1,3-Dibromopropane (1.13 ml),

potassium carbonate (2.30 g), and tetra-n-butylammonium iodide (205 mg) were then added to the solution, and the mixture was heated under reflux for 3 hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(3-bromopropoxy)-3-methylbenzene (1) (831 mg, yield 65%).

[1080] The compound (1) (1.07 g) was dissolved in acetone (5 ml) to prepare a solution. 4-Hydroxythiophenol (647 mg), potassium carbonate (709 mg) were then added to the solution, and the mixture was stirred at room temperature for 2 hr. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-[[3-(3-methylphenoxy)propyl]sulfanyl]phenol (2) (1.00 g, yield 78%).

[1081] Chlorobenzene (0.3 ml) was added to the compound (2) (100 mg) and 4-chloro-6,7-dimethoxyquinazoline (165 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (82 mg, yield 49%).

[1082] The resultant compound (70 mg) was dissolved in a 10% hydrochloric acid-methanol solution (3 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 12 mg of a hydrochloride.

Mass spectrometry value (ESI-MS, m/z): 463 (M⁺+1)

Example 847: 6,7-Dimethoxy-4-(4-[[4-(3-methylphenoxy)butyl]sulfanyl]phenoxy)quinazoline

[1083] m-Cresol (1 g) was dissolved in acetonitrile (3 ml) to prepare a solution. 1,4-Dibromobutane (2.21 ml), potassium carbonate (3.84 g), and tetra-n-butylammonium iodide (342 mg) were then added to the solution, and the mixture was heated under reflux for one hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(4-bromobutoxy)-3-methylbenzene (1).

[1084] The compound (1) was dissolved in acetone (4 ml) to prepare a solution. 4-Hydroxythiophenol (2.07 g) and potassium carbonate (2.27 g) were then added to the solution, and the mixture was stirred at room temperature for 6 hr. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-[[4-(3-methylphenoxy)butyl]-sulfanyl]phenol (2) (1.04 g, yield 39%).

[1085] Chlorobenzene (0.4 ml) was added to the compound (2) (100 mg) and 4-chloro-6,7-dimethoxyquinazoline (156 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (110 mg, yield 66%).

[1086] The resultant compound (95 mg) was dissolved in a 10% hydrochloric acid-methanol solution (8 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 60 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.71 - 1.91 (m, 4H), 2.26 (s, 3H), 3.07 (t, J = 7.1 Hz, 2H), 3.93 - 4.04 (m, 8H), 6.68 - 6.76 (m, 3H), 7.14 (t, J = 8.1 Hz, 1H), 7.25 - 7.31 (m, 2H), 7.38 - 7.48 (m, 3H), 7.59 (s, 1H), 8.64 (s, 1H)

Example 848: 4-(4-[[4-(2-Fluorophenoxy)butyl]sulfanyl]phenoxy)-6,7-dimethoxyquinazoline

[1087] o-Fluorophenol (1.0 g) was dissolved in acetonitrile (3 ml) to prepare a solution. 1,4-Dibromobutane (2.13 ml), potassium carbonate (3.70 g), and tetra-n-butylammonium iodide (330 mg) were then added to the solution, and the mixture was heated under reflux for one hr. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(4-bromobutoxy)-2-fluorobenzene (1) (1.57 g, yield 71%).

[1088] The compound (1) (1.55 g) was dissolved in acetone (4 ml) to prepare a solution. 4-Hydroxythiophenol (873 mg) and potassium carbonate (956 mg) were then added to the solution, and the mixture was stirred at room temperature for 2 hr. 1 N HCl was added to reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-[[3-(2-fluorophenoxy)butyl]sulfanyl]phenol (2) (1.66 g, yield 90%).

[1089] Chlorobenzene (0.4 ml) was added to the compound (2) (100 mg) and 4-chloro-6,7-dimethoxyquinazoline (154 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (117 mg, yield 73%).

[1090] The resultant compound (96 mg) was dissolved in a 10% hydrochloric acid-methanol solution (6 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Ethyl acetate was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 81 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.73 - 1.94 (m, 4H), 3.09 (t, J = 7.3 Hz, 2H), 3.99 (s, 3H), 4.01 (s, 3H), 4.08 (t, J = 6.3 Hz, 2H), 6.87 - 6.96 (m, 1H), 7.07 - 7.22 (m, 3H), 7.27 - 7.32 (m, 2H), 7.43 - 7.48 (m, 3H), 7.61 (s, 1H), 8.71 (s, 1H)

Example 849: 4-(4-[[2-(2-Fluorophenoxy)ethyl]sulfanyl]phenoxy)-6,7-dimethoxyquinazoline

[1091] o-Fluorophenol (0.6 g) was dissolved in acetone (2 ml) to prepare a solution. 1-Bromo-2-chloroethane (0.69 ml), potassium carbonate (1.11 g), and tetra-n-butylammonium iodide (198 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(2-chloroethoxy)-2-fluorobenzene (1) (438 mg, yield 47%).

[1092] The compound (1) (432 mg) was dissolved in acetone (3 ml) to prepare a solution. 4-Hydroxythiophenol (343 mg) and potassium carbonate (376 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-[[2-(2-fluorophenoxy)ethyl]sulfanyl]phenol (2) (345 mg, yield 53%).

[1093] Chlorobenzene (0.4 ml) was added to the compound (2) (100 mg) and 4-chloro-6,7-dimethoxyquinazoline (171 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (110 mg, yield 64%).

[1094] The resultant compound (90 mg) was dissolved in a 10% hydrochloric acid-methanol solution (6 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 60 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.42 (t, J = 6.6 Hz, 2H), 3.98 (s, 3H), 4.00 (s, 3H), 4.26 (t, J = 6.3 Hz, 2H), 6.92 - 6.99 (m, 1H), 7.08 - 7.62 (m, 9H), 8.65 (s, 1H)

Example 850: 6,7-Dimethoxy-4-(4-[[2-(3-methylphenoxy)ethyl]sulfanyl]phenoxy)quinazoline

[1095] m-Cresol (0.6 g) was dissolved in acetone (2 ml) to prepare a solution. 1-Bromo-2-chloroethane (0.69 ml), potassium carbonate (1.15 g), and tetra-n-butylammonium iodide (205 mg) were then added to the solution, and the mixture was heated under reflux overnight. Water was added to the reaction solution, and the mixture was extracted with chloroform. The extract was washed with saturated brine and was dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure, and the residue was purified by chromatography on silica gel using hexane/ethyl acetate for development to give 1-(2-chloroethoxy)-3-methylbenzene (1) (347 mg, yield 37%).

[1096] The compound (1) (341 mg) was dissolved in acetone (3 ml) to prepare a solution. 4-Hydroxythiophenol (278 mg) and potassium carbonate (304 mg) were then added to the solution, and the mixture was stirred at room temperature overnight. 1 N HCl was added to the reaction solution, and the mixture was extracted with chloroform, followed

by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using chloroform for development to give 4-[[2-(3-methylphenoxy)ethyl]sulfanyl]phenol (2) (243 mg, yield 47%).

[1097] Chlorobenzene (0.4 ml) was added to the compound (2) (100 mg) and 4-chloro-6,7-dimethoxyquinazoline (174 mg), and the mixture was stirred at 140°C overnight. A saturated aqueous sodium hydrogencarbonate solution was added to the reaction solution, and the mixture was extracted with chloroform, followed by washing with saturated brine. The extract was then dried over anhydrous sodium sulfate. The solvent was removed by distillation under the reduced pressure. The residue was purified by chromatography on silica gel using hexane/acetone for development to give the title compound (86 mg, yield 50%).

[1098] The resultant compound (72 mg) was dissolved in a 10% hydrochloric acid-methanol solution (6 ml) to prepare a solution which was then allowed to stand at room temperature for 10 min. The solvent was removed by distillation under the reduced pressure. Diethyl ether was then added to the residue, and the precipitated crystal was collected by filtration and was washed to give 52 mg of a hydrochloride.

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.27 (s, 3H), 3.38 (t, J = 6.3 Hz, 2H), 3.98 (s, 3H), 4.00 (s, 3H), 4.17 (t, J = 6.3 Hz, 2H), 6.68 - 6.78 (m, 3H), 7.12 - 7.18 (m, 1H), 7.27 - 7.34 (m, 2H), 7.41 (s, 1H), 7.50 - 7.56 (m, 2H), 7.58 (s, 1H), 8.62 (s, 1H)

Example 851: N-[2-(2,4-Dichlorophenoxy)ethyl]-N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]amine

[1099] Sodium hydride (60 mg) was dissolved in dimethylformamide (3 ml) to prepare a solution. A dimethylformamide solution (5 ml) of 2,4-dichlorophenol (245 mg) was then added to the solution, and the mixture was stirred at room temperature for 10 min. Subsequently, a dimethylformamide solution (5 ml) of bromomethylacetate (344 mg) was added thereto, and the mixture was further stirred at room temperature for 90 min. Water was added to stop the reaction, and the reaction solution was extracted with ethyl acetate, followed by washing with water and saturated brine. The extract was then dried over sodium sulfate. After the concentration of the extract, a 5% aqueous sodium hydroxide solution (10 ml) was added thereto, and the mixture was stirred at 80°C for 10 hr. Subsequently, the solution was acidified by the addition of 1 N hydrochloric acid. The resultant white precipitate was collected by filtration and was dried to give 2-(2,4-dichlorophenoxy)acetic acid (310 mg, yield 94%).

[1100] 2-(2,4-Dichlorophenoxy)acetic acid (310 mg) was added to chloroform (5 ml), and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (403 mg), 1-hydroxybenzotriazole monohydrate (284 mg), and 4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (498 mg) were added thereto. The mixture was then stirred with heating under reflux for 2 hr. A saturated aqueous sodium hydrogencarbonate solution was added to stop the reaction, and the reaction solution was extracted with chloroform, followed by washing with a saturated aqueous sodium hydrogencarbonate solution, 1 N hydrochloric acid, water, and saturated brine. The extract was then dried over sodium sulfate. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give N1-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-2-(2,4-dichlorophenoxy)acetamide (500 mg, yield 72%).

[1101] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-2-(2,4-dichlorophenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (156 mg, yield 80%).

[1102] ¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.76 (t, J = 5.4 Hz, 2H), 4.11 (s, 3H), 4.14 (s, 3H), 4.47 (t, J = 5.4 Hz, 2H), 6.81 (d, J = 6.6 Hz, 1H), 7.08 (d, J = 8.8 Hz, 1H), 7.23 - 7.27 (m, 3H), 7.38 (d, J = 2.7 Hz, 1H), 7.54 (d, J = 8.8 Hz, 2H), 7.69 - 7.70 (m, 1H), 8.01 (s, 1H), 8.65 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 486 (M⁺+1)

Example 852: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N-[2-(2-methylphenoxy)ethyl]amine

[1103] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-2-(2-methylphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.11 (s, 3H), 3.88 (brs, 2H), 4.06 (s, 3H), 4.10 (s, 3H), 4.40 (brs, 2H), 6.72 -

6.76 (m, 3H), 6.96 - 7.01 (m, 2H), 7.28 - 7.32 (m, 2H), 7.53 (s, 1H), 7.88 (s, 1H), 7.96 (brs, 2H), 8.72 (brs, 1H)
Mass spectrometry value (ESI-MS, m/z): 431 (M⁺+1)

Example 853: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N-[2-(2-methoxyphenoxy)ethyl]amine

[1104] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-2-(2-methoxyphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 447 (M⁺+1)

Example 854: N-[2-(2,6-Dichlorophenoxy)ethyl]-N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]amine

[1105] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-2-(2,6-dichlorophenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (156 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.59 (brs, 2H), 4.04 (s, 3H), 4.05 (s, 3H), 4.29 (t, J = 5.4 Hz, 2H), 4.54 (brs, 1H), 6.43 (d, J = 5.4 Hz, 1H), 6.76 (d, J = 9.0 Hz, 2H), 6.98 - 7.05 (m, 3H), 7.27 - 7.31 (m, 3H), 7.41 (s, 1H), 7.59 (s, 1H), 8.46 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 486 (M⁺+1)

Example 855: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N-[2-(2,6-dimethylphenoxy)ethyl]amine

[1106] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-2-(2,6-dimethylphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.29 (s, 6H), 3.55 - 3.56 (m, 2H), 3.99 - 4.02 (m, 2H), 4.03 (s, 3H), 4.04 (s, 3H), 4.38 (brs, 1H), 6.42 (d, J = 5.4 Hz, 1H), 6.76 (d, J = 8.8 Hz, 2H), 6.92 - 7.05 (m, 5H), 7.42 (s, 1H), 7.60 (s, 1H), 8.46 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 445 (M⁺+1)

Example 856: N-[2-(2,6-Dimethoxyphenoxy)ethyl]-N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]amine

[1107] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-2-(2,6-dimethoxyphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.37 - 3.39 (m, 2H), 3.85 (s, 3H), 3.88 (s, 3H), 4.039 (s, 3H), 4.044 (s, 3H), 4.28 (t, J = 5.1 Hz, 2H), 5.01 (brs, 1H), 6.43 (d, J = 5.4 Hz, 1H), 6.57 - 6.61 (m, 2H), 6.72 (d, J = 8.8 Hz, 1H), 7.00 - 7.04 (m, 3H), 7.41 (s, 1H), 7.60 (s, 1H), 8.45 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 477 (M⁺+1)

Example 857: N-[2-(2,6-Difluorophenoxy)ethyl]-N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]amine

[1108] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-2-(2,6-difluorophenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 453 (M⁺+1)

Example 858: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N-[2-(3,5-dimethylphenoxy)ethyl]amine

[1109] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-2-(3,5-dimethylphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 445 (M⁺+1)

Example 859: N-[2-(4-Chlorophenoxy)ethyl]-N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]amine

[1110] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-2-(4-chlorophenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 452 (M⁺+1)

Example 860: N-[2-(3-Chlorophenoxy)ethyl]-N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]amine

[1111] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-2-(3-chlorophenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 452 (M⁺+1)

Example 861: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N-[2-(2-ethylphenoxy)ethyl]amine

[1112] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-2-(2-ethylphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 445 (M⁺+1)

Example 862: N-[4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl]-N-[2-(2-methylphenoxy)ethyl]amine

[1113] N1-[4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl]-2-(2-methylphenoxy)acetamide (200 mg) was dissolved in

tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.26 (s, 3H), 3.58 (t, J = 5.1 Hz, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 4.21 (t, J = 5.4 Hz, 3H), 6.75 - 6.91 (m, 4H), 7.08 - 7.18 (m, 4H), 7.31 (s, 1H), 7.57 (s, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 432 (M⁺+1)

Example 863: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N-[2-(4-methoxyphenoxy)ethyl]amine

[1114] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-2-(4-methoxyphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.52 (t, J = 4.9 Hz, 2H), 3.77 (s, 3H), 4.04 (s, 3H), 4.05 (s, 3H), 4.15 (t, J = 5.1 Hz, 2H), 6.74 (d, J = 8.8 Hz, 2H), 6.83 - 6.89 (m, 4H), 7.03 (d, J = 8.8 Hz, 2H), 7.41 (s, 1H), 7.59 (s, 1H), 8.45 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 447 (M⁺+1)

Example 864: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N-[2-(4-ethylphenoxy)ethyl]amine

[1115] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-2-(4-ethylphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 445 (M⁺+1)

Example 865: N-[2-(2,5-Dichlorophenoxy)ethyl]-N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]amine

[1116] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-2-(2,5-dichlorophenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 486 (M⁺+1)

Example 866: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N-[2-(4-fluorophenoxy)ethyl]amine

[1117] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-2-(4-fluorophenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 4.03 (s, 3H), 4.04 (s, 3H), 4.14 (t, J = 5.4 Hz, 2H), 6.82 - 6.84 (m, 3H), 6.97 - 7.01 (m, 2H), 7.11 - 7.16 (m, 4H), 7.62 (s, 1H), 7.74 (s, 1H), 8.78 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 435 (M⁺+1)

Example 867: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N-[2-(4-fluorophenoxy)ethyl]-N-methylamine

[1118] Dimethylformamide (240 ml) was added to sodium hydride (1.96 g), and N1-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl-2-(4-fluorophenoxy)acetamide (11 g) was added thereto. Subsequently, a dimethylformamide solution (10 ml) of methyl iodide (7 g) was added thereto, and the mixture was stirred at room temperature for 2 hr. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and saturated brine in that order. The extract was then dried over sodium sulfate and was then concentrated, and the residue was purified on a column using hexane/acetone to give N1-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl-N1-methyl-2-(4-fluorophenoxy)acetamide (7.1 g, yield 63%).

[1119] N1-4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl-N1-methyl-2-(4-fluorophenoxy)acetamide (7.1 g) was dissolved in tetrahydrofuran (250 ml) to prepare a solution. A 1 M solution (46 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (3.2 g, yield 40%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.10 (s, 3H), 3.78 (t, J = 5.9 Hz, 2H), 4.07 (s, 3H), 4.08 (s, 3H), 4.14 (t, J = 5.9 Hz, 2H), 6.51 (d, J = 5.6 Hz, 1H), 6.82 - 6.85 (m, 4H), 6.94 - 7.00 (m, 2H), 7.06 - 7.08 (m, 2H), 7.61 (s, 1H), 7.64 (s, 1H), 8.45 (d, J = 5.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 449 (M⁺+1)

Example 868: N-[2-(2-Chlorophenoxy)ethyl]-N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}amine

[1120] N1-4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl-2-(2-chlorophenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 452 (M⁺+1)

Example 869: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N-(2-phenoxyethyl)amine

[1121] N1-4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl-2-phenoxyacetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 417 (M⁺+1)

Example 870: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N-[2-(4-methylphenoxy)ethyl]amine

[1122] N1-4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl-2-(4-methylphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 431 (M⁺+1)

Example 871: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N-[2-(3-methylphenoxy)ethyl]amine

[1123] N1-4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl-2-(3-methylphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

furan was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 431 (M⁺+1)

Example 872: 2-(2-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]anilino}ethoxy)phenol

[1124] N1-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-2-(2-hydroxyphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 4.02 (s, 3H), 4.03 (s, 3H), 4.12 (t, J = 5.4 Hz, 2H), 6.71 - 6.95 (m, 7H), 7.15 - 7.17 (m, 2H), 7.62 (s, 1H), 7.73 (s, 1H), 8.77 (d, J = 6.6 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 433 (M⁺+1)

Example 873: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N-(2-phenoxyethyl)amine

[1125] N1-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-2-phenoxyacetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.56 (t, J = 5.1 Hz, 2H), 4.07 (s, 6H), 4.21 (t, J = 4.9 Hz, 2H), 6.76 (d, J = 8.8 Hz, 2H), 6.93 - 7.00 (m, 3H), 7.09 (d, J = 8.8 Hz, 2H), 7.28 - 7.33 (m, 2H), 7.39 (s, 1H), 7.57 (s, 1H), 8.65 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 418 (M⁺+1)

Example 874: 2-(2-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]anilino}ethoxy)phenol

[1126] N1-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-2-(2-hydroxyphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 3.60 (t, J = 5.4 Hz, 2H), 4.06 (s, 3H), 4.07 (s, 3H), 4.28 (t, J = 5.4 Hz, 2H), 6.78 (d, J = 8.8 Hz, 2H), 6.87 - 6.94 (m, 4H), 7.10 (d, J = 9.0 Hz, 2H), 7.32 (s, 1H), 7.57 (s, 1H), 8.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 434 (M⁺+1)

Example 875: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylphenyl}-N-(2-phenoxyethyl)amine

[1127] N1-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylphenyl}-2-phenoxyacetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 434 (M⁺+1)

Example 876: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylphenyl}-N-[2-(2-methylphenoxy)ethyl]amine

[1128] N1-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylphenyl}-2-(2-methylphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.02 (s, 3H), 2.19 (s, 3H), 3.50 (t, J = 4.9 Hz, 2H), 3.96 (s, 3H), 3.98 (s, 3H), 4.12 (t, J = 4.9 Hz, 2H), 6.23 (d, J = 5.1 Hz, 1H), 6.50 - 6.54 (m, 2H), 6.76 - 6.89 (m, 3H), 7.07 - 7.10 (m, 2H), 7.34 (s, 1H), 7.55 (s, 1H), 8.35 - 8.36 (m, 1H)

Mass spectrometry value (ESI-MS, m/z): 445 (M⁺+1)

Example 877: N-[2-(2-Chlorophenoxy)ethyl]-N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-methylphenyl}amine

[1129] N1-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylphenyl}-2-(2-chlorophenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.10 (s, 3H), 3.60 (t, J = 4.9 Hz, 2H), 4.04 (s, 3H), 4.06 (s, 3H), 4.26 (t, J = 5.1 Hz, 2H), 6.31 (d, J = 5.4 Hz, 1H), 6.59 - 6.65 (m, 2H), 6.91 - 6.97 (m, 3H), 7.20 - 7.22 (m, 1H), 7.38 - 7.40 (m, 1H), 7.42 (s, 1H), 7.63 (s, 1H), 8.43 (d, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 466 (M⁺+1)

Example 878: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylphenyl}-N-[2-(3-methylphenoxy)ethyl]amine

[1130] N1-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylphenyl}-2-(3-methylphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.10 (s, 3H), 2.34 (s, 3H), 3.54 (t, J = 4.9 Hz, 2H), 4.04 (s, 3H), 4.06 (s, 3H), 4.18 (t, J = 5.1 Hz, 2H), 6.30 (d, J = 5.4 Hz, 1H), 6.56 - 6.61 (m, 2H), 6.74 - 6.81 (m, 3H), 6.95 (d, J = 8.3 Hz, 1H), 7.18 (t, J = 7.6 Hz, 1H), 7.42 (s, 1H), 7.63 (s, 1H), 8.43 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 445 (M⁺+1)

Example 879: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylphenyl}-N-[2-(4-methylphenoxy)ethyl]amine

[1131] N1-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylphenyl}-2-(4-methylphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.10 (s, 3H), 2.30 (s, 3H), 3.53 (t, J = 4.9 Hz, 2H), 4.04 (s, 3H), 4.06 (s, 3H), 4.17 (t, J = 5.1 Hz, 2H), 6.30 (d, J = 5.1 Hz, 1H), 6.56 - 6.61 (m, 2H), 6.83 - 6.96 (m, 3H), 7.10 (d, J = 8.5 Hz, 2H), 7.42 (s, 1H), 7.63 (s, 1H), 8.43 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 445 (M⁺+1)

Example 880: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylphenyl}-N-[2-(2-methoxyphenoxy)ethyl]amine

[1132] N1-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylphenyl}-2-(2-methoxyphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.10 (s, 3H), 3.55 (t, J = 4.9 Hz, 2H), 3.89 (s, 3H), 4.04 (s, 3H), 4.06 (s, 3H), 4.25 (t, J = 4.9 Hz, 2H), 6.29 - 6.31 (m, 1H), 6.57 - 6.61 (m, 1H), 6.89 - 7.11 (m, 6H), 7.43 - 7.44 (m, 1H), 7.61 - 7.65 (m, 1H), 8.44 (t, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 460 (M⁺+1)

Example 881: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylphenyl}-N-[2-(2,6-dimethylphenoxy)ethyl]amine

[1133] N1-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylphenyl}-2-(2,6-dimethylphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.11 (s, 3H), 2.30 (s, 6H), 3.55 (t, J = 5.1 Hz, 2H), 4.02 (t, J = 4.9 Hz, 2H), 4.05 (s, 3H), 4.07 (s, 3H), 6.30 (d, J = 5.4 Hz, 1H), 6.60 - 6.64 (m, 2H), 6.94 - 6.98 (m, 2H), 7.02 - 7.04 (m, 2H), 7.43 (s, 1H), 7.63 (s, 1H), 8.44 (t, J = 5.1 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 459 (M⁺+1)

Example 882: N-[2-(2,6-Dimethoxyphenoxy)ethyl]-N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-methylphenyl}amine

[1134] N1-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylphenyl}-2-(2,6-dimethoxyphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (156 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.10 (s, 3H), 3.38 (brs, 2H), 3.89 (s, 6H), 4.05 (s, 3H), 4.06 (s, 3H), 4.27 (t, J = 5.1 Hz, 2H), 4.94 (brs, 1H), 6.31 (d, J = 5.1 Hz, 1H), 6.56 - 6.61 (m, 4H), 6.94 (d, J = 8.5 Hz, 1H), 7.02 (t, J = 8.3 Hz, 1H), 7.43 (s, 1H), 7.64 (s, 1H), 8.44 (t, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 491 (M⁺+1)

Example 883: N-[2-(2,6-Difluorophenoxy)ethyl]-N-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-methylphenyl}amine

[1135] N1-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylphenyl}-2-(2,6-difluorophenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.10 (s, 3H), 3.50 (brs, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 4.37 (t, J = 5.1 Hz, 2H),

6.31 (d, J = 5.4 Hz, 1H), 6.57 - 6.63 (m, 2H), 6.89 - 6.99 (m, 4H), 7.43 (s, 1H), 7.63 (s, 1H), 8.44 (d, J = 5.4 Hz, 1H)
Mass spectrometry value (ESI-MS, m/z): 467 (M⁺+1)

Example 884: N-[2-(2,6-Dimethoxyphenoxy)ethyl]-N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]amine

[1136] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]-2-(2,6-dimethoxyphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (156 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.10 (s, 3H), 2.24 (s, 3H), 3.44 (t, J = 4.4 Hz, 2H), 3.87 (s, 6H), 4.05 (s, 3H), 4.07 (s, 3H), 4.32 (t, J = 4.6 Hz, 2H), 4.72 (brs, 1H), 6.27 (d, J = 5.4 Hz, 1H), 6.58 - 6.62 (m, 3H), 6.91 (d, J = 8.8 Hz, 1H), 7.03 (t, J = 8.5 Hz, 1H), 7.43 (s, 1H), 7.66 (s, 1H), 8.42 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 505 (M⁺+1)

Example 885: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N-(3-phenoxypropyl)amine

[1137] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-3-phenoxypropaneamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.30 - 2.33 (m, 2H), 3.91 (s, 3H), 3.98 (s, 3H), 4.00 (t, J = 5.6 Hz, 2H), 4.34 (t, J = 7.1 Hz, 2H), 6.21 (d, J = 7.6 Hz, 1H), 6.86 - 7.01 (m, 7H), 7.27 - 7.32 (m, 3H), 7.47 (d, J = 7.6 Hz, 1H), 7.83 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 431 (M⁺+1)

Example 886: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]-N-(3-phenoxypropyl)amine

[1138] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]-3-phenoxypropaneamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.08 (s, 3H), 2.14 (s, 3H), 2.17 - 2.23 (m, 2H), 3.43 (t, J = 6.3 Hz, 2H), 4.04 (s, 3H), 4.06 (s, 3H), 4.16 (t, J = 5.9 Hz, 2H), 6.29 (d, J = 5.4 Hz, 1H), 6.54 (s, 1H), 6.82 (s, 1H), 6.93 - 6.97 (m, 3H), 7.28 - 7.32 (m, 2H), 7.43 (s, 1H), 7.62 (s, 1H), 8.42 (d, J = 5.4 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 459 (M⁺+1)

Example 887: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]-N-(3-phenoxypropyl)amine

[1139] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]-3-phenoxypropaneamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

¹H-NMR (CDCl₃-d₁, 400 MHz): δ 2.07 (s, 3H), 2.14 (s, 3H), 2.17 - 2.30 (m, 2H), 3.42 (t, J = 6.3 Hz, 2H), 4.05 (s, 3H), 4.06 (s, 3H), 4.17 (t, J = 5.9 Hz, 2H), 6.26 (d, J = 5.4 Hz, 1H), 6.59 (d, J = 8.5 Hz, 1H), 6.90 - 6.97 (m, 3H), 7.28

- 7.43 (m, 3H), 7.65 (s, 1H), 8.41 (d, J = 5.4 Hz, 1H), 8.58 (d, J = 4.9 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 459 (M⁺+1)

Example 888: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N-[3-(2-methylphenoxy)propyl]amine

[1140] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-3-(2-methylphenoxy)propaneamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 445 (M⁺+1)

Example 889: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]-N-[3-(2-methylphenoxy)propyl]amine

[1141] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]-3-(2-methylphenoxy)propaneamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 473 (M⁺+1)

Example 890: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]-N-[3-(2-methylphenoxy)propyl]amine

[1142] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]-3-(2-methylphenoxy)propaneamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 473 (M⁺+1)

Example 891: N-[3-(2-Chlorophenoxy)propyl]-N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]amine

[1143] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-3-(2-chlorophenoxy)propaneamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 466 (M⁺+1)

Example 892: N-[3-(2-Chlorophenoxy)propyl]-N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]amine

[1144] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]-3-(2-chlorophenoxy)propaneamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (156 mg,

yield 80%).

Mass spectrometry value (ESI-MS, m/z): 494 ($M^{+}+1$)

Example 893: N-[3-(2-Chlorophenoxy)propyl]-N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]amine

[1145] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]-3-(2-chlorophenoxy)propaneamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (156 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 494 ($M^{+}+1$)

Example 894: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]-N-[2-(2,6-dimethylphenoxy)ethyl]amine

[1146] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]-2-(2,6-dimethylphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 473 ($M^{+}+1$)

Example 895: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]-N-[2-(2,6-dimethylphenoxy)ethyl]amine

[1147] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]-2-(2,6-dimethylphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (155 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 473 ($M^{+}+1$)

Example 896: N-[2-(2,6-Dimethoxyphenoxy)ethyl]-N-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]amine

[1148] N1-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,5-dimethylphenyl]-2-(2,6-dimethoxyphenoxy)acetamide (200 mg) was dissolved in tetrahydrofuran (10 ml) to prepare a solution. A 1 M solution (1.3 ml) of a borane-tetrahydrofuran complex in tetrahydrofuran was then added to the solution, and the mixture was stirred with heating under reflux for 2 hr. The reaction solution was cooled to 0°C and was adjusted to pH = 1 by the addition of 1 N hydrochloric acid, followed by stirring with heating under reflux for 30 min. The reaction solution was cooled to 0°C, was adjusted to pH = 12 by the addition of a 1 N aqueous sodium hydroxide solution, and was extracted with chloroform. After the concentration of the extract, the residue was purified on a column using chloroform/methanol to give the title compound (156 mg, yield 80%).

Mass spectrometry value (ESI-MS, m/z): 505 ($M^{+}+1$)

Example 897: N-Benzoyl-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]thiourea

[1149] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 1-benzenecarbonyl isothiocyanate (50 μ l) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (78 mg, yield 94%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.02 (s, 6H), 6.54 (d, J = 5.12 Hz, 1H), 7.22 (d, J = 8.78 Hz, 2H), 7.33 - 7.77 (m, 5H), 7.81 (t, J = 3.42 Hz, 1H), 7.83 - 7.95 (m, 3H), 8.02 (d, J = 8.76 Hz, 1H), 8.49 (d, J = 5.12 Hz, 1H), 9.42 (bs, 1H)
Mass spectrometry value (ESI-MS, m/z): 460 (M⁺+1)

5 Example 898: N-(2-Chlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1150] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 2-chloro-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (83 mg, yield 100%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.07 (s, 6H), 6.57 (d, J = 5.37 Hz, 1H), 7.23 - 7.29 (m, 3H), 7.44 - 7.47 (m, 2H), 7.53 - 7.54 (m, 3H), 7.79 - 7.86 (m, 3H), 8.53 (d, J = 5.37 Hz, 1H), 9.23 (s, 1H)
Mass spectrometry value (ESI-MS, m/z): 494 (M⁺+1)

15 Example 899: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-fluorobenzoyl)thiourea

[1151] 2-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-fluoro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (75 mg, yield 93%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.06 (s, 6H), 6.57 (d, J = 5.37 Hz, 1H), 7.23 - 7.29 (m, 5H), 7.39 (m, 1H), 7.44 (s, 1H), 7.54 (s, 1H), 7.64 - 7.67 (m, 1H), 7.83 (d, J = 9.03 Hz, 2H), 8.13 (m, 1H), 8.53 (d, J = 5.37 Hz, 1H)
Mass spectrometry value (ESI-MS, m/z): 478 (M⁺+1)

25 Example 900: N-(2-Bromobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1152] 2-Bromo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-bromo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml). A solution of 2-bromo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (85 mg, yield 93%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.93 (s, 3H), δ 3.95 (s, 3H), 6.56 (d, J = 5.12 Hz, 1H), 7.32 (d, J = 8.30 Hz, 2H), 7.41 (d, J = 5.61 Hz, 2H), 7.44 - 7.52 (m, 3H), 7.62 (t, J = 7.19 Hz, 1H), 7.72 (d, J = 7.81 Hz, 1H), 7.84 (d, J = 8.78 Hz, 2H), 8.31 (s, 1H), 8.52 (s, 1H)
Mass spectrometry value (ESI-MS, m/z): 539 (M⁺+1)

40 Example 901: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-methoxybenzoyl)thiourea

[1153] 2-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-methoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (83 mg, yield 96%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.11 (s, 3H), 4.13 (s, 3H), 4.17 (s, 3H), 6.77 (d, J = 6.01 Hz, 1H), 7.19 (t, J = 7.69 Hz, 1H), 7.26 - 7.29 (m, 6H), 7.61 - 7.65 (m, 2H), 7.99 (d, J = 8.78 Hz, 1H), 8.13 (s, 1H), 8.24 (dd, J = 1.83 Hz, J = 7.93 Hz, 1H), 8.51 (m, 1H)
Mass spectrometry value (ESI-MS, m/z): 490 (M⁺+1)

55 Example 902: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-[2-(trifluoromethyl)benzoyl]thiourea

[1154] 2-(Trifluoromethyl)-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-(trifluoromethyl)-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solu-

tion. A solution of 2-(trifluoromethyl)-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (83 mg, yield 95%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.93 (s, 3H), 3.95 (s, 3H), 6.56 (d, J = 5.12 Hz, 1H), 7.32 (d, J = 8.78 Hz, 2H), 7.40 (s, 1H), 7.49 (s, 1H), 7.75 - 7.86 (m, 6H), 8.51 (d, J = 5.12 Hz, 1H), 12.13 (s, 1H), 12.33 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 528 (M⁺+1)

Example 903: N-Benzoyl-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}thiourea

[1155] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (76 mg, yield 80%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.04 (s, 3H), 4.06 (s, 3H), 6.64 (d, J = 5.12 Hz, 1H), 7.04 - 7.07 (m, 2H), 7.26 (s, 2H), 7.45 (s, 1H), 7.48 (s, 1H), 7.57 (t, J = 7.69 Hz, 1H), 7.68 (t, J = 7.44 Hz, 1H), 7.93 (d, J = 7.39 Hz, 2H), 8.46 (t, J = 8.79 Hz, 1H), 8.57 (d, J = 5.12 Hz, 1H), 9.22 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 478 (M⁺+1)

Example 904: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-(2-methylbenzoyl)thiourea

[1156] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 2-methyl-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (66 mg, yield 85%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.58 (s, 3H), 4.08 (s, 3H), 4.12 (s, 3H), 6.72 (d, J = 5.61 Hz, 1H), 7.08 - 7.12 (m, 2H), 7.26 - 7.36 (m, 3H), 7.47 - 7.59 (m, 3H), 7.82 (bs, 1H), 8.56 (d, J = 5.85 Hz, 1H), 8.60 (m, 1H), 8.93 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

Example 905: N-(2-Chlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}thiourea

[1157] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 2-chloro-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (63 mg, yield 80%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.04 (s, 3H), 4.06 (s, 3H), 6.64 (d, J = 5.37 Hz, 1H), 7.04 - 7.08 (m, 2H), 7.27 (s, 1H), 7.43 - 7.47 (m, 3H), 7.53 - 7.55 (m, 2H), 7.83 (d, J = 7.32 Hz, 1H), 8.48 (t, J = 8.90 Hz, 1H), 8.57 (d, J = 5.37 Hz, 1H), 9.39 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 512 (M⁺+1)

Example 906: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-(2-fluorobenzoyl)thiourea

[1158] 2-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-fluoro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (63 mg, yield 80%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.11 (s, 3H), 4.17 (s, 3H), 6.84 (d, J = 6.59 Hz, 1H), 7.06 - 7.15 (m, 3H), 7.33 - 7.40 (m, 3H), 7.58 - 7.68 (m, 1H), 8.13 (bs, 2H), 8.58 (d, J = 6.59 Hz, 1H), 8.73 (bs, 1H), 10.00 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 496 (M⁺+1)

Example 907: N-(2-Bromobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}thiourea

[1159] 2-Bromo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-bromo-1-benzene-

carbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-bromo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (73 mg, yield 83%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.92 (s, 3H), 3.96 (s, 3H), 6.67 (d, J = 5.12 Hz, 1H), 7.16 (d, J = 8.78 Hz, 1H), 7.37 - 7.52 (m, 5H), 7.62 (d, J = 7.07 Hz, 1H), 7.72 (d, J = 7.56 Hz, 1H), 8.11 (t, J = 8.53 Hz, 1H), 8.55 (d, J = 5.12 Hz, 1H), 12.20 (s, 1H), 12.26 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 557 (M⁺+1)

Example 908: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl]-N'-(2-iodobenzoyl)thiourea

[1160] 2-Iodo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-iodo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-iodo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (86 mg, yield 90%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.93 (s, 3H), 3.96 (s, 3H), 6.66 (d, J = 5.21 Hz, 1H), 7.14 (d, J = 7.56 Hz, 1H), 7.26 (t, J = 5.61 Hz, 1H), 7.34 - 7.53 (m, 5H), 7.93 (d, J = 8.35 Hz, 1H), 8.16 (m, 1H), 8.54 (d, J = 5.21 Hz, 1H), 12.14 (bs, 1H), 12.32 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 604 (M⁺+1)

Example 909: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl]-N'-(2-methoxybenzoyl)thiourea

[1161] 2-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-methoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (56 mg, yield 70%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.93 (s, 3H), 3.96 (s, 3H), 4.03 (s, 3H), 6.67 (d, J = 5.37 Hz, 1H), 7.11 - 7.47 (m, 4H), 7.58 (m, 1H), 7.68 (m, 1H), 7.78 (m, 1H), 7.93 (d, J = 6.34 Hz, 1H), 8.14 (m, 1H), 8.56 (d, J = 5.37 Hz, 1H), 11.39 (s, 1H), 12.44 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 508 (M⁺+1)

Example 910: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl]-N'-[2-(trifluoromethyl)benzoyl]thiourea

[1162] 2-(Trifluoromethyl)-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-(trifluoromethyl)-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-(trifluoromethyl)-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (69 mg, yield 80%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.93 (s, 3H), 3.96 (s, 3H), 6.67 (d, J = 5.12 Hz, 1H), 7.13 (m, 1H), 7.42 - 7.47 (m, 3H), 7.69 - 7.85 (m, 4H), 8.12 (m, 1H), 8.56 (d, J = 5.12 Hz, 1H), 12.17 (s, 1H), 12.31 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 546 (M⁺+1)

Example 911: N-Benzoyl-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]thiourea

[1163] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (64 mg, yield 85%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.09 (s, 3H), 4.10 (s, 3H), 6.59 (d, J = 5.85 Hz, 1H), 7.27 (s, 1H), 7.34 (t, J = 8.54

Hz, 1H), 7.54 - 7.61 (m, 4H), 7.68 - 7.72 (m, 2H), 7.92 (d, J = 7.80 Hz, 2H), 8.01 (d, J = 11.47 Hz, 1H), 8.53 (d, J = 5.85 Hz, 1H), 9.13 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 478 (M⁺+1)

5 Example 912: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]-N'-(2-methylbenzoyl)thiourea

[1164] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 2-methyl-1-benzenecarbonyl isothiocyanate (50 µl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (55 mg, yield 70%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.58 (s, 3H), 4.11 (s, 3H), 4.16 (s, 3H), 6.71 (d, J = 6.34 Hz, 1H), 7.36 (s, 1H), 7.37 - 7.40 (m, 3H), 7.50 (t, J = 7.81 Hz, 1H), 7.57 - 7.64 (m, 3H), 8.06 (bs, 1H), 8.17 (d, J = 9.50 Hz, 1H), 8.54 (d, J = 6.34 Hz, 1H), 8.88 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

Example 913: N-(2-Chlorobenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]thiourea

[1165] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 2-chloro-1-benzenecarbonyl isothiocyanate (50 µl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (61 mg, yield 75%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.06 (s, 3H), 4.07 (s, 3H), 6.48 (d, J = 5.12 Hz, 1H), 7.26 (s, 1H), 7.31 (t, J = 8.42 Hz, 1H), 7.44 - 7.58 (m, 6H), 7.79 (d, J = 7.56 Hz, 1H), 8.03 (d, J = 11.47 Hz, 1H), 8.53 (d, J = 5.12 Hz, 1H), 9.33 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 512 (M⁺+1)

Example 914: N-(2-Bromobenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]thiourea

[1166] 2-Bromo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-bromo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-bromo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (73 mg, yield 83%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.96 (s, 6H), 6.51 (d, J = 5.12 Hz, 1H), 7.42 - 7.53 (m, 7H), 7.59 - 7.63 (m, 2H), 7.72 (d, J = 7.80 Hz, 1H), 8.10 (d, J = 8.10 Hz, 1H), 8.51 (d, J = 8.51 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 557 (M⁺+1)

Example 915: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]-N'-(2-iodobenzoyl)thiourea

[1167] 2-Iodo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-iodo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-iodo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (86 mg, yield 90%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.25 (s, 6H), 6.50 (d, J = 4.64 Hz, 1H), 7.11 (t, J = 1.71 Hz, 1H), 7.24 - 7.52 (m, 6H), 7.61 (d, J = 9.03 Hz, 1H), 7.84 (d, J = 8.05 Hz, 1H), 7.93 (d, J = 8.05 Hz, 1H), 8.14 (d, J = 12.2 Hz, 1H), 8.49 (d, J = 5.12 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 604 (M⁺+1)

Example 916: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]-N'-(2-methoxybenzoyl)thiourea

[1168] 2-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-methoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the

mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (65 mg, yield 80%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 4.03 (s, 9H), 6.95 (d, J = 6.01 Hz, 1H), 7.18 (t, J = 7.56 Hz, 1H), 7.31 (d, J = 8.54 Hz, 1H), 7.53 (s, 1H), 7.63 - 7.75 (m, 4H), 7.93 (d, J = 6.34 Hz, 1H), 8.21 (d, J = 12.4 Hz, 1H), 8.83 (d, J = 6.59 Hz, 1H), 11.35 (s, 1H), 12.72 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 508 (M⁺+1)

Example 917: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}-N'-[2-(trifluoromethyl)benzoyl]thiourea

[1169] 2-(Trifluoromethyl)-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-(trifluoromethyl)-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-(trifluoromethyl)-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (63 mg, yield 73%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.96 (s, 3H), 3.97 (s, 3H), 6.53 (d, J = 6.34 Hz, 1H), 7.43 (s, 1H), 7.52 (t, J = 9.15 Hz, 2H), 7.62 - 7.64 (m, 1H), 7.75 - 7.84 (m, 3H), 7.87 - 7.88 (m, 1H), 8.09 (d, J = 14.6 Hz, 1H), 8.52 (d, J = 5.37 Hz, 1H), 12.23 (bs, 1H), 12.37 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 546 (M⁺+1)

Example 918: N-Benzoyl-N'-{3-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1170] 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (63 mg, yield 85%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.03 (s, 3H), 4.07 (s, 3H), 6.45 (d, J = 5.37 Hz, 1H), 7.26 (s, 2H), 7.29 (d, J = 8.78 Hz, 1H), 7.56 - 7.60 (m, 3H), 7.69 (t, J = 7.44 Hz, 1H), 7.74 (dd, J = 2.68 Hz, J = 8.78 Hz, 1H), 7.92 (d, J = 7.08 Hz, 2H), 8.11 (s, 1H), 8.57 (bs, 1H), 9.17 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 494 (M⁺+1)

Example 919: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-methylbenzoyl)thiourea

[1171] 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 2-methyl-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (69 mg, yield 90%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.51 (s, 3H), 4.06 (s, 3H), 4.07 (s, 3H), 6.42 (d, J = 5.37 Hz, 1H), 7.28 - 7.36 (m, 4H), 7.47 - 7.59 (m, 4H), 7.75 (dd, J = 2.44 Hz, 8.78 Hz, 1H), 8.11 (d, J = 2.44 Hz, 1H), 8.50 (d, J = 5.37 Hz, 1H), 8.92 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 509 (M⁺+1)

Example 920: N-(2-Chlorobenzoyl)-N'-{3-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}thiourea

[1172] 3-Chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 2-chloro-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (79 mg, yield 90%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 6.43 (d, J = 5.12 Hz, 1H), 7.43 - 7.59 (m, 5H), 7.64 (d, J = 7.81 Hz, 1H), 7.76 (d, J = 11.22 Hz, 1H), 8.19 (bs, 1H), 8.52 (d, 1H, J = 5.37 Hz), 12.12 (bs, 1H), 12.38 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 530 (M⁺+1)

Example 921: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-fluorobenzoyl)thiourea

[1173] 2-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-fluoro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (66 mg, yield 86%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 6.43 (d, J = 5.12 Hz, 1H), 7.34 - 7.39 (m, 2H), 7.43 (s, 1H), 7.51 (t, J = 9.15 Hz, 2H), 7.56 - 7.69 (m, 3H), 8.17 (bs, 1H), 8.52 (d, J = 5.37 Hz, 1H), 11.79 (bs, 1H), 12.43 (bs, 1H)
Mass spectrometry value (ESI-MS, m/z): 512 (M⁺+1)

Example 922: N-(2-Bromobenzoyl)-N'-{3-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1174] 2-Bromo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-bromo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-bromo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (61 mg, yield 70%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 6.43 (d, J = 5.12 Hz, 1H), 7.32 - 7.53 (m, 5H), 7.60 (d, J = 5.86 Hz, 1H), 7.72 - 7.76 (m, 2H), 8.20 (bs, 1H), 8.51 (d, J = 5.12 Hz, 1H), 12.12 (s, 1H), 12.39 (s, 1H)
Mass spectrometry value (ESI-MS, m/z): 573 (M⁺+1)

Example 923: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-methoxybenzoyl)thiourea

[1175] 2-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-methoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (67 mg, yield 85%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 4.03 (s, 3H), 6.43 (d, J = 5.37 Hz, 1H), 7.19 (t, J = 7.32 Hz, 1H), 7.31 (d, J = 8.05 Hz, 1H), 7.43 (s, 1H), 7.49 - 7.54 (m, 3H), 7.68 (t, J = 8.78 Hz, 1H), 7.78 (dd, J = 2.68 Hz, J = 9.03 Hz, 1H), 7.93 (d, J = 9.76 Hz, 1H), 8.52 (d, J = 5.13 Hz, 1H), 11.33 (bs, 1H), 2.59 (bs, 1H)
Mass spectrometry value (ESI-MS, m/z): 525 (M⁺+1)

Example 924: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-[2-(trifluoromethyl)benzoyl]-thiourea

[1176] 2-(Trifluoromethyl)-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-(trifluoromethyl)-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-(trifluoromethyl)-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (61 mg, yield 85%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 6.42 (d, J = 5.02 Hz, 1H), 7.42 (s, 1H), 7.48 (d, J = 8.78 Hz, 1H), 7.53 (s, 1H), 7.75 - 7.87 (m, 6H), 8.19 (bs, 1H), 8.50 (d, J = 5.12 Hz, 1H), 12.21 (s, 1H)
Mass spectrometry value (ESI-MS, m/z): 562 (M⁺+1)

Example 925: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-nitrophenyl]-N'-(2-methylbenzoyl)thiourea

[1177] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-nitroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 2-methyl-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (66 mg, yield 80%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.36 (s, 3H), 3.93 (s, 3H), 3.94 (s, 3H), 6.52 (d, J = 5.37 Hz, 1H), 7.15 - 7.22 (m, 3H), 7.28 - 7.39 (m, 3H), 7.42 (dd, J = 2.81 Hz, 9.15 Hz, 1H), 7.50 (s, 1H), 7.54 (s, 1H), 7.66 (bs, 1H), 7.81 (s, 1H), 8.46 (d, J = 5.12 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 519 (M⁺+1)

Example 926: N-Benzoyl-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}thiourea

[1178] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (69 mg, yield 89%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.09 (s, 3H), 4.11 (s, 3H), 7.23 - 7.34 (m, 4H), 7.55 - 7.59 (m, 4H), 7.68 (t, J = 7.56 Hz, 1H), 7.88 - 7.93 (m, 3H), 8.69 (s, 1H), 9.12 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 461 (M⁺+1)

Example 927: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(2-methylbenzoyl)thiourea

[1179] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 2-methyl-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (72 mg, yield 90%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.50 (s, 3H), 3.98 (s, 3H), 3.99 (s, 3H), 7.29 - 7.38 (m, 7H), 7.42 - 7.46 (m, 1H), 7.52 (d, J = 7.81 Hz, 1H), 7.57 (s, 1H), 7.80 - 7.82 (m, J = 8.78 Hz, 2H), 8.56 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 475 (M⁺+1)

Example 928: N-(2-Chlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}thiourea

[1180] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 2-chloro-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (79 mg, yield 95%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.98 (s, 3H), 3.99 (s, 3H), 7.37 - 7.40 (m, 3H), 7.45 - 7.49 (m, 1H), 7.53 - 7.58 (m, 3H), 7.65 (d, J = 7.81 Hz, 1H), 7.79 (d, J = 8.54 Hz, 2H), 8.58 (s, 1H), 12.04 (bs, 1H), 12.35 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 495 (M⁺+1)

Example 929: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(2-methoxybenzoyl)thiourea

[1181] 2-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-methoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (74 mg, yield 90%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.97 (s, 3H), 4.03 (s, 3H), 4.05 (s, 3H), 6.81 (d, J = 6.34 Hz, 1H), 7.11 - 7.12 (m, 1H), 7.17 - 7.23 (m, 2H), 7.31 (d, J = 8.54 Hz, 1H), 7.53 - 7.80 (m, 3H), 7.88 (dd, J = 2.56 Hz, 8.91 Hz, 1H), 7.81 (d, J = 7.81 Hz, 1H), 8.30 (s, 1H), 8.81 (d, J = 6.34 Hz, 1H), 11.4 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 491 (M⁺+1)

Example 930: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(3-methylbenzoyl)thiourea

[1182] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 3-methyl-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (77 mg, yield 96%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.48 (s, 3H), 4.08 (s, 3H), 4.11 (s, 3H), 6.65 (d, J = 5.85 Hz, 1H), 7.23 - 7.29 (m, 2H), 7.43 - 7.58 (m, 3H), 7.61 (s, 1H), 7.72 (t, J = 8.66 Hz, 3H), 7.89 (d, J = 8.78 Hz, 2H), 8.51 (d, J = 5.85 Hz, 1H), 9.13 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 474 (M⁺+1)

Example 931: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(3-fluorobenzoyl)thiourea

[1183] 3-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-fluoro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (70 mg, yield 87%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.05 (s, 3H), 4.06 (s, 3H), 6.57 (d, J = 5.12 Hz, 1H), 7.24 - 7.26 (m, 3H), 7.35 - 7.40 (m, 1H), 7.44 (s, 1H), 7.54 - 7.59 (m, 2H), 7.64 - 7.68 (m, 2H), 7.80 - 7.84 (m, 2H), 8.53 (d, J = 5.12 Hz, 1H), 9.09 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 478 (M⁺+1)

Example 932: N-(3-Chlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1184] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 3-chloro-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (77 mg, yield 93%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.05 (s, 3H), 4.06 (s, 3H), 6.58 (d, J = 5.37 Hz, 1H), 7.24 - 7.92 (m, 11H), 8.52 (d, J = 5.37 Hz, 1H), 9.13 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 494 (M⁺+1)

Example 933: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(3-methoxybenzoyl)thiourea

[1185] 3-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-methoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (70 mg, yield 80%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.90 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), 6.57 (d, J = 5.37 Hz, 1H), 7.13 - 7.16 (m, 2H), 7.23 - 7.26 (m, 2H), 7.37 - 7.49 (m, 4H), 7.54 (s, 1H), 7.81 - 7.84 (m, 2H), 8.53 (d, J = 5.37 Hz, 1H), 9.13 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 490 (M⁺+1)

Example 934: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-[3-(trifluoromethyl)benzoyl]thiourea

[1186] 3-(Trifluoromethyl)-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-(trifluoromethyl)-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-(trifluoromethyl)-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (67 mg, yield 75%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.94 (s, 3H), 3.96 (s, 3H), 6.59 (d, J = 5.37 Hz, 1H), 7.35 (d, J = 8.78 Hz, 2H), 7.43 (s, 1H), 7.53 (s, 1H), 7.78 - 7.85 (m, 3H), 8.04 (d, J = 8.05 Hz, 1H), 8.26 (d, J = 8.05 Hz, 1H), 8.35 (s, 1H), 8.55 (d, J = 5.37 Hz, 1H), 11.79 (s, 1H), 12.49 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 528 (M⁺+1)

Example 935: N-(3-Bromobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1187] 3-Bromo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-bromo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-bromo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (67 mg, yield 75%).

carbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-bromo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (67 mg, yield 74%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.05 (s, 3H), 4.06 (s, 3H), 6.66 (d, J = 5.12 Hz, 1H), 7.24 - 7.26 (m, 3H), 7.44 - 7.47 (m, 2H), 7.53 (s, 1H), 7.80 - 7.84 (m, 4H), 8.07 (bs, 1H), 8.53 (d, J = 5.12 Hz, 1H), 9.03 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 539 (M⁺+1)

Example 936: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-(3-methylbenzoyl)thiourea

[1188] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 3-methyl-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (68 mg, yield 87%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.47 (s, 3H), 4.04 (s, 3H), 4.06 (s, 3H), 6.64 (d, J = 5.12 Hz, 1H), 7.03 - 7.07 (m, 2H), 7.26 (s, 2H), 7.42 - 7.49 (m, 3H), 7.07 - 7.73 (m, 2H), 8.46 (t, J = 8.90 Hz, 1H), 8.57 (d, J = 5.12 Hz, 1H), 9.18 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

Example 937: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-(3-fluorobenzoyl)thiourea

[1189] 3-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-fluoro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (71 mg, yield 90%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.93 (s, 3H), 3.96 (s, 3H), 6.67 (d, J = 5.37 Hz, 1H), 7.38 - 7.73 (m, 6H), 7.84 - 7.86 (m, 1H), 8.05 (m, 2H), 8.29 (s, 1H), 8.56 (d, J = 5.12 Hz, 1H), 11.9 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 496 (M⁺+1)

Example 938: N-(3-Chlorobenzoyl)-N'-(4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl)thiourea

[1190] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 3-chloro-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (76 mg, yield 93%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.04 (s, 3H), 4.06 (s, 3H), 6.63 (d, J = 5.13 Hz, 1H), 6.65 - 7.07 (m, 2H), 7.26 - 7.27 (m, 1H), 7.45 - 7.53 (m, 3H), 7.65 (d, J = 8.05 Hz, 1H), 7.80 (d, J = 8.78 Hz, 1H), 7.94 (s, 1H), 8.44 (t, J = 7.93 Hz, 1H), 8.57 (d, J = 5.13 Hz, 1H), 9.17 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 512 (M⁺+1)

Example 939: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-(3-methoxybenzoyl)thiourea

[1191] 3-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-methoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (73 mg, yield 90%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.86 (s, 3H), 3.93 (s, 3H), 3.96 (s, 3H), 6.66 (d, J = 5.12 Hz, 1H), 7.16 (d, J = 7.32 Hz, 1H), 7.22 - 7.24 (m, 1H), 7.38 - 7.48 (m, 4H), 7.57 - 7.60 (m, 2H), 8.08 (t, J = 8.91 Hz, 1H), 8.56 (d, J = 5.12 Hz, 1H), 11.82 (bs, 1H), 12.55 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 508 (M⁺+1)

Example 940: N-(3-Bromobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}thiourea

[1192] 3-Bromo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-bromo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-bromo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (85 mg, yield 96%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.93 (s, 3H), 3.96 (s, 3H), 6.66 (d, J = 4.88 Hz, 1H), 7.15 (d, J = 9.51 Hz, 1H), 7.36 - 7.39 (m, 2H), 7.41 (s, 1H), 7.46 (s, 1H), 7.51 (t, J = 7.81 Hz, 1H), 7.86 (d, J = 7.81 Hz, 1H), 7.98 (d, J = 7.56 Hz, 1H), 8.07 (m, 1H), 8.19 (s, 1H), 8.70 (d, J = 5.12 Hz, 1H), 11.98 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 557 (M⁺+1)

Example 941: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}-N'-(3-methylbenzoyl)thiourea

[1193] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 3-methyl-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (64 mg, yield 82%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.48 (s, 3H), 4.06 (s, 3H), 4.07 (s, 3H), 6.49 (d, J = 4.39 Hz, 1H), 7.26 (s, 1H), 7.30 (t, J = 8.54 Hz, 1H), 7.44 - 7.52 (m, 4H), 7.58 (s, 1H), 7.69 - 7.12 (m, 2H), 8.03 (dd, J = 2.44 Hz, 11.71 Hz, 1H), 8.53 (d, J = 5.37 Hz, 1H), 9.13 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

Example 942: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}-N'-(3-fluorobenzoyl)thiourea

[1194] 3-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-fluoro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (65 mg, yield 83%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.10 (s, 3H), 4.15 (s, 3H), 6.68 (d, J = 6.01 Hz, 1H), 7.27 (m, 2H), 7.35 - 7.42 (m, 2H), 7.57 - 7.69 (m, 4H), 7.98 (bs, 1H), 8.12 (m, 1H), 8.54 (d, J = 6.34 Hz, 1H), 9.11 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 496 (M⁺+1)

Example 943: N-(3-Chlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}thiourea

[1195] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 3-chloro-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (73 mg, yield 90%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.09 (s, 3H), 4.11 (s, 3H), 6.60 (d, J = 5.61 Hz, 1H), 7.26 (s, 1H), 7.35 (t, J = 8.54 Hz, 1H), 7.51 - 7.56 (m, 2H), 7.61 (s, 1H), 7.65 - 7.68 (m, 1H), 7.77 - 7.79 (m, 2H), 7.91 - 7.92 (m, 1H), 8.08 (dd, J = 2.68 Hz, 11.47 Hz, 1H), 8.53 (d, J = 5.61 Hz, 1H), 9.08 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 512 (M⁺+1)

Example 944: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}-N'-(3-methoxybenzoyl)thiourea

[1196] 3-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-methoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (73 mg, yield 90%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.99 (s, 3H), 4.13 (s, 3H), 4.17 (s, 3H), 6.87 (d, J = 5.61 Hz, 1H), 7.18 (dd, J = 2.44 Hz, 8.29 Hz, 1H), 7.31 - 7.46 (m, 2H), 7.55 - 7.62 (m, 4H), 7.71 (s, 1H), 7.84 (s, 1H), 8.23 (dd, J = 2.44 Hz, 11.95 Hz, 1H), 8.67 (d, J = 6.59 Hz, 1H), 11.00 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 508 (M⁺+1)

Example 945: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}-N'-[3-(trifluoromethyl)benzoyl]thiourea

[1197] 3-(Trifluoromethyl)-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-(trifluoromethyl)-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-(trifluoromethyl)-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (77 mg, yield 89%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.96 (s, 6H), 6.54 (d, J = 5.37 Hz, 1H), 7.43 (s, 1H), 7.53 - 7.60 (m, 4H), 7.80 (t, J = 8.05 Hz, 1H), 8.02 - 8.10 (m, 2H), 8.26 (d, J = 7.81 Hz, 1H), 8.35 (s, 1H), 8.53 (d, J = 4.88 Hz, 1H), 12.03 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 546 (M⁺+1)

Example 946: N-(3-Bromobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}thiourea

[1198] 3-Bromo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-bromo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-bromo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (79 mg, yield 90%).

¹H-NMR (DMSO-d₆, 400 MHz) : δ 3.96 (s, 6H), 6.51 (d, J = 5.37 Hz, 1H), 7.41 (s, 1H), 7.48 - 7.60 (m, 5H), 7.86 (d, J = 7.56 Hz, 1H), 7.97 (d, J = 8.05 Hz, 1H), 8.08 (d, J = 12.44 Hz, 1H), 8.18 (s, 1H), 8.50 (d, J = 5.37 Hz, 1H), 11.84 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 557 (M⁺+1)

Example 947: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(3-methylbenzoyl)thiourea

[1199] 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 3-methyl-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (71 mg, yield 92%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.48 (s, 3H), 4.07 (s, 6H), 6.44 (d, J = 5.61 Hz, 1H), 7.26 (s, 3H), 7.29 (d, J = 8.78 Hz, 1H), 7.43 - 7.50 (m, 2H), 7.59 (s, 1H), 7.69 - 7.74 (m, 3H), 8.11 (d, J = 2.44 Hz, 1H), 9.14 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 509 (M⁺+1)

Example 948: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(3-fluorobenzoyl)thiourea

[1200] 3-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-fluoro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (64 mg, yield 83%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 6.43 (d, J = 5.12 Hz, 1H), 7.43 (s, 3H), 7.49 - 7.54 (m, 2H), 7.59 - 7.62 (m, 1H), 7.75 (d, J = 8.78 Hz, 1H), 7.82 - 7.86 (m, 1H), 8.18 (bs, 1H), 8.51 (d, J = 5.12 Hz, 1H), 11.79 (bs, 1H), 12.43 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 512 (M⁺+1)

Example 949: N-(3-Chlorobenzoyl)-N'-[3-chloro-4-(6,7-dimethoxy-4-quinolyl)oxy]phenyl]thiourea

[1201] 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml)

to prepare a solution. Commercially available 3-chloro-1-benzenecarbonyl isothiocyanate (50 μ l) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (77 mg, yield 97%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.06 (s, 3H), 4.07 (s, 3H), 6.46 (d, J = 5.37 Hz, 1H), 7.29 - 7.32 (m, 4H), 7.52 (t, J = 7.93 Hz, 1H), 7.61 (s, 1H), 7.64 - 7.66 (m, 1H), 7.71 (dd, J = 2.68 Hz, 8.78 Hz, 1H), 7.87 (d, J = 7.81 Hz, 1H), 8.00 (s, 1H), 8.07 (d, J = 2.44 Hz, 1H), 8.51 (d, J = 5.37 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 529 (M⁺+1)

Example 950: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(3-methoxybenzoyl)thiourea

[1202] 3-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-methoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (65 mg, yield 82%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.86 (s, 3H), 3.95 (s, 3H), 3.96 (s, 3H), 6.41 (d, J = 5.12 Hz, 1H), 7.22 (d, J = 8.54 Hz, 1H), 7.41 - 7.60 (m, 8H), 7.74 (d, J = 8.78 Hz, 1H), 8.12 (bs, 1H), 8.50 (d, J = 5.37 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 525 (M⁺+1)

Example 951: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-[3-(trifluoromethyl)benzoyl]thiourea

[1203] 3-(Trifluoromethyl)-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-(trifluoromethyl)-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-(trifluoromethyl)-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (75 mg, yield 88%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 6.43 (d, J = 5.37 Hz, 1H), 7.42 (s, 1H), 7.49 - 7.53 (m, 2H), 7.74 (d, J = 9.27 Hz, 1H), 7.80 (t, J = 8.05 Hz, 1H), 8.03 (d, J = 7.56 Hz, 1H), 8.18 (s, 1H), 8.26 (d, J = 5.37 Hz, 1H), 8.35 (s, 1H), 8.51 (d, J = 5.37 Hz, 1H), 12.04 (s, 1H), 12.52 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 562 (M⁺+1)

Example 952: N-(3-Bromobenzoyl)-N'-(3-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl)thiourea

[1204] 3-Bromo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-bromo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-bromo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (81 mg, yield 93%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 4.05 (s, 3H), 4.06 (s, 3H), 6.85 (d, J = 6.34 Hz, 1H), 7.50 - 7.54 (m, 2H), 7.66 (d, J = 8.78 Hz, 1H), 7.76 (s, 1H), 7.85 - 7.89 (m, 2H), 7.98 (d, J = 7.80 Hz, 1H), 8.19 (s, 1H), 8.28 (s, 1H), 8.84 (d, J = 6.34 Hz, 1H), 11.8 (s, 1H), 12.56 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 573 (M⁺+1)

Example 953: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-nitrophenyl}-N'-(3-methylbenzoyl)thiourea

[1205] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-nitroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 3-methyl-1-benzenecarbonyl isothiocyanate (50 μ l) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (69 mg, yield 91%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.47 (s, 3H), 4.04 (s, 3H), 4.07 (s, 3H), 6.67 (d, J = 5.37 Hz, 1H), 7.26 (s, 2H), 7.43 - 7.51 (m, 4H), 7.73 (d, J = 7.32 Hz, 1H), 7.77 (s, 1H), 7.94 (d, J = 2.68 Hz, 1H), 8.52 (d, J = 9.03 Hz, 1H), 8.61 (d, J

= 5.12 Hz, 1H), 9.24 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 519 (M⁺+1)

Example 954: N-[4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl]-N'-(3-methylbenzoyl)thiourea

[1206] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 3-methyl-1-benzenecarbonyl isothiocyanate (50 μ l) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (76 mg, yield 95%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.47 (s, 3H), 4.12 (s, 3H), 4.17 (s, 3H), 7.26 - 7.34 (m, 5H), 7.45 - 7.47 (m, 1H), 7.61 (s, 1H), 7.71 (m, 2H), 7.93 (d, J = 9.03 Hz, 2H), 8.77 (s, 1H), 9.10 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 475 (M⁺+1)

Example 955: N-(3-Chlorobenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]thiourea

[1207] 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 3-chloro-1-benzenecarbonyl isothiocyanate (50 μ l) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (80 mg, yield 96%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.08 (s, 6H), 7.29 (s, 2H), 7.33 (d, J = 8.78 Hz, 1H), 7.41 (s, 1H), 7.50 (t, J = 7.81 Hz, 1H), 7.57 (s, 1H), 7.63 (d, J = 7.32 Hz, 1H), 7.83 - 7.86 (m, 3H), 7.98 (s, 1H), 8.65 (s, 1H), 9.71 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 495 (M⁺+1)

Example 956: N-[4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl]-N'-(3-methoxybenzoyl)thiourea

[1208] 3-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-methoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (67 mg, yield 81%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.87 (s, 3H), 3.98 (s, 3H), 3.99 (s, 3H), 7.21 - 7.23 (m, 1H), 7.28 - 7.39 (m, 3H), 7.46 (t, J = 7.93 Hz, 1H), 7.56 - 7.60 (m, 3H), 7.79 (d, J = 8.78 Hz, 2H), 8.56 (s, 1H), 11.59 (s, 1H), 12.66 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 491 (M⁺+1)

Example 957: N-[4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl]-N'-[3-(trifluoromethyl)benzoyl]thiourea

[1209] 3-(Trifluoromethyl)-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-(trifluoromethyl)-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-(trifluoromethyl)-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (75 mg, yield 85%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.97 (s, 3H), 3.99 (s, 3H), 7.38 - 7.44 (m, 3H), 7.58 (s, 1H), 7.78 - 7.82 (m, 3H), 8.04 (d, J = 8.05 Hz, 1H), 8.26 (d, J = 7.81 Hz, 1H), 8.36 (s, 1H), 8.56 (s, 1H), 11.97 (s, 1H), 12.95 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 529 (M⁺+1)

Example 958: N-(3-Bromobenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]thiourea

[1210] 3-Bromo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-bromo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-bromo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (61 mg, yield 70%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.98 (s, 3H), 3.99 (s, 3H), 7.37 - 7.40 (m, 3H), 7.52 (t, J = 7.93 Hz, 1H), 7.58 (s, 1H), 7.78 (d, J = 8.78 Hz, 2H), 7.87 (d, J = 7.08 Hz, 1H), 7.97 (d, J = 7.81 Hz, 1H), 8.18 (s, 1H), 8.58 (s, 1H), 11.89 (bs, 1H), 12.48 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 540 (M⁺+1)

Example 959: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(4-methylbenzoyl)thiourea

[1211] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 4-methyl-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (70 mg, yield 89%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.48 (s, 3H), 4.09 (s, 3H), 4.15 (s, 3H), 6.72 (d, J = 6.34 Hz, 1H), 7.23 - 7.29 (m, 3H), 7.37 (d, J = 7.81 Hz, 2H), 7.62 (s, 1H), 7.82 (d, J = 8.05 Hz, 2H), 7.94 (d, J = 9.03 Hz, 2H), 7.98 (s, 1H), 8.51 (d, J = 5.12 Hz, 1H), 9.12 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 474 (M⁺+1)

Example 960: N-(4-Chlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1212] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 4-chloro-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (77 mg, yield 92%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.06 (s, 3H), 4.07 (s, 3H), 6.59 (d, J = 5.37 Hz, 1H), 7.24 - 7.30 (m, 3H), 7.46 - 7.56 (m, 4H), 7.76 - 7.88 (m, 4H), 8.53 (d, J = 5.37 Hz, 1H), 9.08 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 494 (M⁺+1)

Example 961: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(4-fluorobenzoyl)thiourea

[1213] 4-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-fluoro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (69 mg, yield 85%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.05 (s, 3H), 4.06 (s, 3H), 6.57 (d, J = 5.12 Hz, 1H), 7.24 - 7.26 (m, 5H), 7.44 (s, 1H), 7.54 (s, 1H), 7.80 - 7.83 (m, 2H), 7.95 (m, 2H), 8.53 (d, J = 5.37 Hz, 1H), 9.09 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 478 (M⁺+1)

Example 962: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(4-nitrobenzoyl)thiourea

[1214] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 4-nitro-1-benzenecarbonyl isothiocyanate (30 mg) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (80 mg, yield 94%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.06 (s, 3H), 4.08 (s, 3H), 6.59 (d, J = 5.37 Hz, 1H), 7.24 - 7.30 (m, 5H), 7.50 (s, 1H), 7.54 (s, 1H), 7.82 - 7.85 (m, 2H), 8.01 - 8.12 (m, 2H), 8.41 - 8.43 (m, 2H), 8.53 (d, J = 5.37 Hz, 1H), 9.16 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 507 (M⁺+1)

Example 963: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(4-methoxybenzoyl)thiourea

[1215] 4-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-methoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chroma-

tography on silica gel using chloroform/acetone for development to give the title compound (67 mg, yield 81%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.92 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), 6.57 (d, J = 5.37 Hz, 1H), 7.02 - 7.04 (m, 2H), 7.23 - 7.26 (m, 3H), 7.44 (s, 1H), 7.54 (s, 1H), 7.77 - 7.85 (m, 2H), 7.88 - 7.90 (m, 2H), 8.53 (d, J = 5.37 Hz, 1H), 9.07 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 490 (M⁺+1)

Example 964: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-(4-methylbenzoyl)thiourea

[1216] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 4-methyl-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (77 mg, yield 98%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.47 (s, 3H), 4.04 (s, 3H), 4.06 (s, 3H), 6.64 (d, J = 5.37 Hz, 1H), 7.04 - 7.07 (m, 2H), 7.26 (s, 1H), 7.36 (d, J = 8.54 Hz, 2H), 7.46 (d, J = 11.95 Hz, 2H), 7.83 (d, J = 8.29 Hz, 2H), 8.46 (t, J = 8.90 Hz, 1H), 8.56 (d, J = 5.12 Hz, 1H), 9.18 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 492 (M⁺+1)

Example 965: N-(4-Chlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}thiourea

[1217] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 4-chloro-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (77 mg, yield 94%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.04 (s, 3H), 4.06 (s, 3H), 6.64 (d, J = 5.12 Hz, 1H), 7.04 - 7.07 (m, 2H), 7.26 (s, 1H), 7.45 - 7.46 (m, 2H), 7.54 - 7.56 (m, 2H), 7.87 - 7.89 (m, 2H), 8.39 (t, J = 8.78 Hz, 1H), 8.57 (d, J = 5.37 Hz, 1H), 9.17 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 512 (M⁺+1)

Example 966: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-(4-fluorobenzoyl)thiourea

[1218] 4-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-fluoro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (65 mg, yield 83%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.93 (s, 3H), 3.96 (s, 3H), 6.62 (d, J = 5.37 Hz, 1H), 7.17 (d, J = 11.2 Hz, 1H), 7.36 - 7.47 (m, 5H), 8.05 - 8.11 (m, 3H), 8.56 (d, J = 5.12 Hz, 1H), 11.88 (s, 1H), 12.48 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 496 (M⁺+1)

Example 967: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-(4-iodobenzoyl)thiourea

[1219] 4-Iodo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-iodo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-iodo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (92 mg, yield 96%).

¹H-NMR (DMSO-d₆, 400 MHz) : δ 3.96 (s, 3H), 4.03 (s, 3H), 6.67 (d, J = 4.88 Hz, 1H), 7.17 (d, J = 8.29 Hz, 2H), 7.39 - 7.47 (m, 2H), 7.77 (d, J = 8.05 Hz, 2H), 7.94 (d, J = 8.29 Hz, 2H), 8.06 (t, J = 8.54 Hz, 1H), 8.56 (d, J = 5.12 Hz, 1H), 11.90 (s, 1H), 12.44 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 604 (M⁺+1)

Example 968: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-(4-nitrobenzoyl)thiourea

[1220] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml)

to prepare a solution. Commercially available 4-nitro-1-benzenecarbonyl isothiocyanate (30 mg) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (75 mg, yield 90%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.04 (s, 3H), 4.06 (s, 3H), 6.64 (dd, J = 3.42 Hz, J = 5.12 Hz, 1H), 7.05 - 7.08 (m, 2H), 7.25 - 7.26 (m, 2H), 7.45 (dd, J = 3.17 Hz, 6.59 Hz, 2H), 8.12 (dd, J = 2.93 Hz, 8.66 Hz, 2H), 8.39 - 8.45 (m, 3H), 8.57 (dd, J = 3.42 Hz, J = 5.12 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 523 (M⁺+1)

Example 969: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl]-N'-(4-methoxybenzoyl)thiourea

[1221] 4-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-methoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (71 mg, yield 88%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.92 (s, 3H), 4.04 (s, 3H), 4.02 (s, 3H), 6.64 (d, J = 5.12 Hz, 1H), 7.02 - 7.06 (m, 4H), 7.26 (s, 1H), 7.46 (d, J = 12.06 Hz, 2H), 7.90 (d, J = 9.03 Hz, 2H), 8.46 (t, J = 9.03 Hz, 1H), 8.56 (d, J = 5.12 Hz, 1H), 9.14 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 508 (M⁺+1)

Example 970: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]-N'-(4-methylbenzoyl)thiourea

[1222] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 4-methyl-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (77 mg, yield 98%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.46 (s, 3H), 4.09 (s, 3H), 4.10 (s, 3H), 6.57 (d, J = 5.37 Hz, 1H), 7.26 - 7.38 (m, 4H), 7.54 (d, J = 8.54 Hz, 1H), 7.59 (s, 1H), 7.68 (s, 1H), 7.81 (d, J = 8.29 Hz, 2H), 8.08 (dd, J = 2.47 Hz, J = 11.47 Hz, 1H), 8.53 (d, J = 5.61 Hz, 1H), 9.09 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

Example 971: N-(4-Chlorobenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]thiourea

[1223] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 4-chloro-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (78 mg, yield 96%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.06 (s, 3H), 4.07 (s, 3H), 6.49 (d, J = 5.12 Hz, 1H), 7.26 (s, 1H), 7.31 (t, J = 8.66 Hz, 1H), 7.44 (s, 1H), 7.50 (d, J = 8.78 Hz, 1H), 7.55 - 7.57 (m, 3H), 7.86 - 7.88 (m, 2H), 8.00 (dd, J = 2.44 Hz, J = 11.47 Hz, 1H), 8.52 (d, J = 5.12 Hz, 1H), 9.11 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 512 (M⁺+1)

Example 972: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]-N'-(4-fluorobenzoyl)thiourea

[1224] 4-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-fluoro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (68 mg, yield 86%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.11 (s, 3H), 4.15 (s, 3H), 6.68 (d, J = 6.34 Hz, 1H), 7.25 - 7.29 (m, 3H), 7.37 (t, J = 8.54 Hz, 1H), 7.58 (d, J = 9.76 Hz, 1H), 7.63 (s, 1H), 7.95 - 7.98 (m, 3H), 8.12 (dd, J = 2.56 Hz, J = 11.59 Hz, 1H), 8.54 (d, J = 6.01 Hz, 1H), 9.09 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 496 ($M^+ + 1$)

Example 973: N-(4-Bromobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}thiourea

[1225] 4-Bromo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-bromo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-bromo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (81 mg, yield 91%).

$^1\text{H-NMR}$ ($\text{DMSO}-d_6$, 400 MHz): δ 3.96 (s, 6H), 6.52 (d, $J = 5.37$ Hz, 1H), 7.42 (s, 1H), 7.49 - 7.59 (m, 3H), 7.76 (d, $J = 8.54$ Hz, 2H), 7.94 (d, $J = 8.54$ Hz, 2H), 8.08 (d, $J = 11.95$ Hz, 1H), 8.51 (d, $J = 5.12$ Hz, 1H), 11.79 (s, 1H), 12.61 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 557 ($M^+ + 1$)

Example 974: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}-N'-(4-iodobenzoyl)thiourea

[1226] 4-Iodo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-iodo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-iodo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (84 mg, yield 88%).

$^1\text{H-NMR}$ ($\text{DMSO}-d_6$, 400 MHz): δ 3.96 (s, 5H), 6.52 (d, $J = 5.37$ Hz, 1H), 7.42 - 7.61 (m, 5H), 7.77 (d, $J = 7.07$ Hz, 2H), 7.85 (d, $J = 8.29$ Hz, 2H), 8.11 (d, $J = 8.54$ Hz, 3H), 8.51 (d, $J = 5.37$ Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 604 ($M^+ + 1$)

Example 975: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}-N'-(4-nitrobenzoyl)thiourea

[1227] 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 4-nitro-1-benzenecarbonyl isothiocyanate (30 mg) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (79 mg, yield 96%).

$^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ 4.11 (s, 3H), 4.17 (s, 3H), 6.75 (m, 1H), 7.29 (s, 2H), 7.40 (t, $J = 8.54$ Hz, 1H), 7.57 (m, 1H), 7.65 (s, 1H), 7.94 (s, 1H), 8.10 (d, $J = 11.47$ Hz, 1H), 8.18 - 8.21 (m, 2H), 8.40 - 8.43 (m, 2H), 8.62 (d, $J = 6.34$ Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 523 ($M^+ + 1$)

Example 976: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}-N'-(4-methoxybenzoyl)thiourea

[1228] 4-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-methoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (70 mg, yield 87%).

$^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ 3.87 (s, 3H), 3.96 (s, 6H), 6.52 (d, $J = 5.12$ Hz, 1H), 7.09 (d, $J = 8.78$ Hz, 2H), 7.43 (s, 1H), 7.49 - 7.54 (m, 2H), 7.61 (d, $J = 8.78$ Hz, 1H), 8.03 - 8.11 (m, 3H), 8.52 (d, $J = 5.37$ Hz, 1H), 11.52 (bs, 1H), 12.82 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 523 ($M^+ + 1$)

Mass spectrometry value (ESI-MS, m/z): 508 ($M^+ + 1$)

Example 977: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(4-methylbenzoyl)thiourea

[1229] 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 4-methyl-1-benzenecarbonyl isothiocyanate (50 μl) was then added to

the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (76 mg, yield 99%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.47 (s, 3H), 4.07 (s, 6H), 6.43 (d, J = 5.37 Hz, 1H), 7.26 (s, 2H), 7.29 (d, J = 8.78 Hz, 2H), 7.37 (d, J = 8.05 Hz, 2H), 7.59 (s, 1H), 7.73 (dd, J = 2.44 Hz, J = 8.78 Hz, 1H), 7.81 (d, J = 8.29 Hz, 2H), 8.10 (d, J = 2.44 Hz, 1H), 9.13 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 509 (M⁺+1)

Example 978: N-(4-Chlorobenzoyl)-N'-[3-chloro-4-(6,7-dimethoxy-4-quinolyl)oxy]phenyl]thiourea

[1230] 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 4-chloro-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (74 mg, yield 93%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.04 (s, 3H), 4.07 (s, 3H), 6.44 (d, J = 5.37 Hz, 1H), 7.29 - 7.32 (m, 3H), 7.54 - 7.60 (m, 4H), 7.71 (dd, J = 2.68 Hz, J = 8.78 Hz, 1H), 7.93 - 7.95 (m, 2H), 8.07 (d, J = 2.44 Hz, 1H), 8.53 (d, J = 5.34 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 529 (M⁺+1)

Example 979: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(4-fluorobenzoyl)thiourea

[1231] 4-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-fluoro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (67 mg, yield 87%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.06 (s, 3H), 4.07 (s, 3H), 6.42 (d, J = 5.37 Hz, 1H), 7.05 - 7.29 (m, 4H), 7.45 (s, 1H), 7.58 (s, 1H), 7.71 (dd, J = 2.44 Hz, J = 8.78 Hz, 1H), 7.94 - 7.98 (m, 2H), 8.08 (d, J = 2.44 Hz, 1H), 8.52 (d, J = 5.37 Hz, 1H), 9.12 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 512 (M⁺+1)

Example 980: N-(4-Bromobenzoyl)-N'-[3-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]thiourea

[1232] 4-Bromo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-bromo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-bromo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (80 mg, yield 83%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 6.43 (d, J = 5.12 Hz, 1H), 7.43 (s, 1H), 7.51 (d, J = 8.54 Hz, 1H), 7.54 (s, 1H), 7.65 - 7.85 (m, 3H), 7.93 (d, J = 8.54 Hz, 2H), 8.31 (bs, 1H), 8.51 (d, J = 5.12 Hz, 1H), 11.81 (bs, 1H), 12.53 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 573 (M⁺+1)

Example 981: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(4-iodobenzoyl)thiourea

[1233] 4-Iodo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-iodo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-iodo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (94 mg, yield 90%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 6.43 (d, J = 5.12 Hz, 1H), 7.43 (s, 1H), 7.49 - 7.54 (m, 2H), 7.66 (d, J = 8.05 Hz, 1H), 7.75 - 7.77 (m, 2H), 7.89 - 7.96 (m, 2H), 8.18 (s, 1H), 8.51 (d, J = 5.37 Hz, 1H), 11.77 (s, 1H), 12.54 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 620 (M⁺+1)

Example 982: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(4-nitrobenzoyl)thiourea

[1234] 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 4-nitro-1-benzenecarbonyl isothiocyanate (30 mg) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (78 mg, yield 95%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.08 (s, 6H), 6.45 (d, J = 5.37 Hz, 1H), 7.31 - 7.33 (m, 3H), 7.46 (s, 1H), 7.61 (s, 1H), 7.69 - 7.72 (m, 1H), 8.07 (d, J = 2.44 Hz, 1H), 8.19 - 8.21 (m, 2H), 8.39 - 8.42 (m, 2H), 8.48 (d, J = 5.37 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 539 (M⁺+1)

Example 983: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(4-methoxybenzoyl)thiourea

[1235] 4-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-methoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (68 mg, yield 86%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.92 (s, 3H), 4.08 (s, 6H), 6.47 (d, J = 5.61 Hz, 1H), 7.04 - 7.05 (m, 2H), 7.31 - 7.34 (m, 3H), 7.52 (bs, 1H), 7.62 (s, 1H), 7.73 (dd, J = 2.44 Hz, 8.78 Hz, 1H), 7.97 (d, J = 9.03 Hz, 2H), 8.09 (d, J = 2.68 Hz, 1H), 8.50 (d, J = 5.38 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 524 (M⁺+1)

Example 984: N-[4-[(6,7-Dimethoxy-4-quinazolinyloxy]phenyl]-N'-(4-methylbenzoyl)thiourea

[1236] 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 4-methyl-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (73 mg, yield 92%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.47 (s, 3H), 4.09 (s, 3H), 4.12 (s, 3H), 7.26 - 7.37 (m, 5H), 7.58 - 7.62 (m, 2H), 7.81 (d, J = 8.29 Hz, 2H), 7.89 (d, J = 8.93 Hz, 2H), 8.69 (s, 1H), 9.09 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 475 (M⁺+1)

Example 985: N-(4-Chlorobenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl]thiourea

[1237] 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 4-chloro-1-benzenecarbonyl isothiocyanate (50 μl) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (82 mg, yield 98%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.98 (s, 3H), 3.99 (s, 3H), 7.36 - 7.40 (m, 3H), 7.58 - 7.63 (m, 3H), 7.78 (d, J = 8.54 Hz, 2H), 8.01 (d, J = 8.29 Hz, 2H), 8.58 (s, 1H), 11.71 (bs, 1H), 12.50 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 495 (M⁺+1)

Example 986: N-[4-[(6,7-Dimethoxy-4-quinazolinyloxy]phenyl]-N'-(4-fluorobenzoyl)thiourea

[1238] 4-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-fluoro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (64 mg, yield 80%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.98 (s, 3H), 3.99 (s, 3H), 7.36 - 7.40 (m, 5H), 7.57 (s, 1H), 7.79 (d, J = 8.78 Hz, 2H), 8.07 - 8.11 (m, 2H), 8.57 (s, 1H), 11.65 (s, 1H), 12.58 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 479 (M⁺+1)

Example 987: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(4-nitrobenzoyl)thiourea

[1239] 4-Nitro-1-benzenecarbonyl isothiocyanate (30 mg) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (74 mg, yield 87%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.11 (s, 3H), 4.14 (s, 3H), 7.26 (s, 1H), 7.34 (d, J = 8.78 Hz, 2H), 7.59 (s, 1H), 7.72 (bs, 1H), 7.89 (d, J = 8.78 Hz, 2H), 8.12 (d, J = 8.78 Hz, 2H), 8.42 (d, J = 8.41 Hz, 2H), 8.72 (s, 1H), 9.19 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 506 (M⁺+1)

Example 988: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(4-methoxybenzoyl)thiourea

[1240] 4-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-methoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (71 mg, yield 86%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.95 (s, 3H), 4.09 (s, 3H), 4.12 (s, 3H), 7.03 (d, J = 9.03 Hz, 2H), 7.26 - 7.33 (m, 3H), 7.58 - 7.63 (m, 2H), 7.89 (d, J = 9.03 Hz, 4H), 8.69 (s, 1H), 9.05 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 491 (M⁺+1)

Example 989: N-(1,3-Benzodioxol-5-ylcarbonyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1241] 1,3-Benzodioxole-5-carbonyl isothiocyanate was prepared using commercially available 1,3-benzodioxole-5-carbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 1,3-benzodioxole-5-carbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (68 mg, yield 86%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.93 (s, 3H), 3.95 (s, 3H), 6.15 (s, 2H), 6.56 (d, J = 5.37 Hz, 1H), 7.08 (d, J = 8.29 Hz, 1H), 7.32 (d, J = 8.78 Hz, 2H), 7.41 (s, 1H), 7.51 (s, 1H), 7.52 (s, 1H), 7.67 (d, J = 8.30 Hz, 1H), 7.82 (d, J = 8.54 Hz, 2H), 8.52 (d, J = 5.37 Hz, 1H), 11.39 (bs, 1H), 12.65 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 504 (M⁺+1)

Example 990: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}-N'-(4-ethoxybenzoyl)thiourea

[1242] 4-Ethoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-ethoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-ethoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (76 mg, yield 92%).

Mass spectrometry value (ESI-MS, m/z): 554 (M⁺+1)

Example 991: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}-N'-(4-phenylbenzoyl)thiourea

[1243] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-phenylbenzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-phenyl-1-benzenecarbonyl isothiocyanate was prepared using the resultant 4-phenyl-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-phenyl-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (76 mg, yield 92%).

Mass spectrometry value (ESI-MS, m/z) : 554 (M⁺+1)

Example 992: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(4-ethoxybenzoyl)thiourea

[1244] 4-Ethoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-ethoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-ethoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (72 mg, yield 89%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.38 (t, J = 6.95 Hz, 3H), 3.95 (s, 3H), 3.96 (s, 3H), 4.14 (dd, J = 7.08 Hz, 13.93 Hz, 2H), 6.41 (d, J = 5.12 Hz, 1H), 7.05 (d, J = 8.78 Hz, 2H), 7.42 (s, 1H), 7.47 (d, J = 8.78 Hz, 1H), 7.53 (s, 2H), 7.26 - 7.75 (m, 1H), 8.02 (d, J = 8.78 Hz, 2H), 8.19 (bs, 1H), 8.50 (d, J = 5.37 Hz, 1H), 11.51 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 539 (M⁺+1)

Example 993: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-(4-ethylbenzoyl)thiourea

[1245] 4-Ethyl-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-ethyl-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-ethyl-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (69 mg, yield 87%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.21 - 1.24 (m, 3H), 2.69 - 2.72 (m, 2H), 3.93 (s, 3H), 3.96 (s, 3H), 6.65 (m, 1H), 7.14 (m, 1H), 7.38 - 7.47 (m, 7H), 7.95 - 7.97 (m, 2H), 8.11 (m, 1H), 8.55 - 8.56 (m, 1H)

Mass spectrometry value (ESI-MS, m/z): 506 (M⁺+1)

Example 994: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-(4-propylbenzoyl)thiourea

[1246] 4-Propyl-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-propyl-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-propyl-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (74 mg, yield 90%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.92 (t, J = 7.08 Hz, 3H), 1.63 - 1.65 (m, 2H), 2.66 (m, 2H), 3.93 (s, 3H), 3.96 (s, 3H), 6.67 (m, 1H), 7.17 (m, 1H), 7.36 - 7.47 (m, 5H), 7.95 (d, J = 8.05 Hz, 2H), 8.09 (m, 1H), 8.31 (s, 1H), 8.55 (d, J = 5.37 Hz, 1H), 11.71 (s, 1H), 12.59 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 520 (M⁺+1)

Example 995: N-(4-Butylbenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}thiourea

[1247] 4-Butyl-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-butyl-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-butyl-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (68 mg, yield 80%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.92 (t, J = 7.44 Hz, 3H), 1.30 - 1.36 (m, 2H), 1.58 - 1.62 (m, 2H), 2.68 (t, J = 7.69 Hz, 3H), 3.93 (s, 3H), 3.96 (s, 3H), 6.57 (d, J = 5.12 Hz, 1H), 7.16 (d, J = 9.27 Hz, 1H), 7.36 - 7.47 (m, 5H), 7.95 (d, J = 8.29 Hz, 2H), 8.11 (t, J = 9.03 Hz, 1H), 8.29 (s, 1H), 8.55 (d, J = 5.37 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 534 (M⁺+1)

Example 996: N-[4-(Chloromethyl)benzoyl]-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}thiourea

[1248] 4-(Chloromethyl)-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-(chloromethyl)-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-(chloromethyl)-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the

solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (68 mg, yield 80%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.96 (s, 3H), 3.99 (s, 3H), 4.44 - 4.45 (m, 2H), 6.76 (d, J = 5.61 Hz, 1H), 7.22 (d, J = 5.61 Hz, 1H), 7.46 - 7.60 (m, 4H), 7.93 - 7.95 (m, 1H), 8.03 - 8.05 (m, 1H), 8.14 (m, 1H), 8.34 (s, 1H), 8.65 (d, J = 5.61 Hz, 1H), 11.88 (s, 1H), 12.55 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 526 (M⁺+1)

Example 997: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]-N'-(4-ethylbenzoyl)thiourea

[1249] 4-Ethyl-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-ethyl-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-ethyl-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (68 mg, yield 84%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.23 (t, J = 7.50 Hz, 3H), 2.71 (dd, J = 7.56 Hz, J = 15.13 Hz, 2H), 3.96 (s, 6H), 6.51 (d, J = 4.88 Hz, 1H), 7.39 (d, J = 8.29 Hz, 2H), 7.42 (s, 1H), 7.50 (t, J = 8.90 Hz, 1H), 7.54 (s, 1H), 7.61 (d, J = 9.27 Hz, 1H), 7.95 (d, J = 8.05 Hz, 2H), 8.10 (d, J = 10.25 Hz, 1H), 8.51 (d, J = 5.37 Hz, 1H), 11.40 (s, 1H), 12.50 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 506 (M⁺+1)

Example 998: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]-N'-(4-propylbenzoyl)thiourea

[1250] 4-Propyl-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-propyl-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-propyl-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (71 mg, yield 86%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.89 - 0.93 (m, 3H), 1.63 - 1.65 (m, 2H), 2.66 (m, 2H), 3.96 (s, 6H), 6.52 (m, 1H), 7.37 - 7.61 (m, 6H), 7.95 (d, J = 6.83 Hz, 2H), 8.11 (m, 1H), 8.51 (d, J = 5.12 Hz, 1H), 11.59 (s, 1H), 12.76 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 520 (M⁺+1)

Example 999: N-(4-Butylbenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]thiourea

[1251] 4-Butyl-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-butyl-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-butyl-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (66 mg, yield 78%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.92 (t, J = 7.20 Hz, 3H), 1.32 - 1.36 (m, 2H), 1.58 - 1.62 (m, 2H), 2.68 (t, J = 7.32 Hz, 2H), 3.96 (s, 6H), 6.51 (d, J = 5.37 Hz, 1H), 7.36 - 7.59 (m, 7H), 7.94 (d, J = 8.05 Hz, 2H), 8.10 (d, J = 12.9 Hz, 1H), 8.30 (s, 1H), 8.51 (d, J = 5.37 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 534 (M⁺+1)

Example 1000: N-[4-(Chloromethyl)benzoyl]-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]thiourea

[1252] 4-(Chloromethyl)-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-(chloromethyl)-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-(chloromethyl)-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (68 mg, yield 81%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 4.02 (s, 6H), 4.45 (s, 2H), 6.84 (m, 1H), 7.54 - 7.70 (m, 6H), 8.03 (d, J = 6.83 Hz, 2H), 8.19 (m, 2H), 8.74 (m, 1H), 11.75 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 526 (M⁺+1)

Example 1001: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(4-propylbenzoyl)thiourea

[1253] 4-Propyl-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-propyl-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-propyl-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (47 mg, yield 58%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.92 - 0.96 (m, 3H), 1.64 - 1.69 (m, 2H), 2.65 - 2.69 (m, 2H), 4.03 (s, 3H), 4.05 (s, 3H), 6.76 (bs, 1H), 7.34 - 7.36 (m, 3H), 7.70 - 7.72 (m, 1H), 7.81 - 7.83 (m, 1H), 7.96 - 8.01 (m, 3H), 8.23 (s, 1H), 8.28 (s, 1H), 11.08 (s, 1H), 11.57 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 537 (M⁺+1)

Example 1002: N-[4-(Chloromethyl)benzoyl]-N'-[4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl]thiourea

[1254] 4-(Chloromethyl)-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-(chloromethyl)-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-(chloromethyl)-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (77 mg, yield 90%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.98 (s, 3H), 3.99 (s, 3H), 4.44 (d, J = 5.86 Hz, 2H), 7.36 - 7.39 (m, 2H), 7.54 - 7.59 (m, 4H), 7.78 - 7.81 (m, 2H), 7.94 (d, J = 8.29 Hz, 2H), 8.03 (d, J = 8.29 Hz, 2H), 8.57 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 509 (M⁺+1)

Example 1003: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2,4-dimethylbenzoyl)thiourea

[1255] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2,4-dimethylbenzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2,4-dimethyl-1-benzenecarbonyl isothiocyanate was prepared using the resultant 2,4-dimethyl-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2,4-dimethyl-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (77 mg, yield 93%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.45 (s, 3H), 2.49 (s, 3H), 3.94 (s, 3H), 3.96 (s, 3H), 6.51 - 6.57 (m, 1H), 7.08 - 7.11 (m, 1H), 7.25 - 7.50 (m, 7H), 7.83 - 7.84 (m, 2H), 8.46 - 8.51 (m, 1H), 11.59 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 488 (M⁺+1)

Example 1004: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2,5-dimethylbenzoyl)thiourea

[1256] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2,5-dimethylbenzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2,5-dimethyl-1-benzenecarbonyl isothiocyanate was prepared using the resultant 2,5-dimethyl-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2,5-dimethyl-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (75 mg, yield 91%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.33 (s, 3H), 2.39 (s, 3H), 3.93 (s, 3H), 3.96 (s, 3H), 6.56 (d, J = 5.37 Hz, 1H), 7.18 - 7.36 (m, 7H), 7.39 (s, 1H), 7.50 (s, 1H), 7.83 - 7.86 (m, 2H), 8.51 (d, J = 5.12 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 488 (M⁺+1)

Example 1005: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2,3-dimethylbenzoyl)thiourea

[1257] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2,3-dimethylbenzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2,3-dimethyl-

1-benzenecarbonyl isothiocyanate was prepared using the resultant 2,3-dimethyl-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml), and a solution of 2,3-dimethyl-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (81 mg, yield 98%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.31 (s, 6H), 3.95 (s, 3H), 3.96 (s, 3H), 6.42 (d, J = 5.36 Hz, 1H), 7.19 (t, J = 7.40 Hz, 1H), 7.29 - 7.34 (m, 4H), 7.41 (s, 1H), 7.48 (d, J = 8.78 Hz, 1H), 7.53 (s, 1H), 7.44 - 7.78 (m, 1H), 8.22 - 8.24 (m, 1H), 11.82 (s, 1H), 12.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 488 (M⁺+1)

Example 1006: N-(2,4-Difluorobenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]thiourea

[1258] 2,4-Difluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-difluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2,4-Difluoro-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (69 mg, yield 82%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.92 (s, 3H), 3.94 (s, 3H), 6.55 (d, J = 5.12 Hz, 1H), 7.22 - 7.27 (m, 2H), 7.32 (d, J = 9.08 Hz, 2H), 7.40 - 7.47 (m, 2H), 7.49 (s, 1H), 7.79 - 7.83 (m, 1H), 8.51 (d, J = 5.12 Hz, 1H), 11.76 (s, 1H), 12.30 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 496 (M⁺+1)

Example 1007: N-(2,6-Difluorobenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]thiourea

[1259] 2,6-Difluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,6-difluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2,6-Difluoro-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (62 mg, yield 74%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.93 (s, 3H), 3.94 (s, 3H), 6.44 (d, J = 5.12 Hz, 1H), 6.84 - 6.87 (m, 1H), 7.02 - 7.25 (m, 4H), 7.37 - 7.49 (m, 2H), 7.59 - 7.63 (m, 2H), 7.80 (bs, 1H), 8.09 (bs, 1H), 8.45 (d, J = 5.37 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 496 (M⁺+1)

Example 1008: N-(2,4-Dichlorobenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]thiourea

[1260] 2,4-Dichloro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-dichloro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2,4-Dichloro-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (70 mg, yield 78%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.05 (s, 3H), 4.06 (s, 3H), 6.57 (d, J = 5.37 Hz, 1H), 7.26 (s, 1H), 7.35 (dd, J = 2.19 Hz, J = 8.42 Hz, 1H), 7.44 - 7.46 (m, 2H), 7.54 - 7.56 (m, 2H), 7.76 - 7.84 (m, 4H), 8.53 (d, J = 5.37 Hz, 1H), 9.29 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 529 (M⁺+1)

Example 1009: N-(3,5-Dichlorobenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]thiourea

[1261] 3,5-Dichloro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3,5-dichloro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3,5-Dichloro-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (73 mg, yield 79%).

Mass spectrometry value (ESI-MS, m/z): 529 (M⁺+1)

Example 1010: N-(3,4-Dimethoxybenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1262] 3,5-Dimethoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3,5-dimethoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3,4-Dimethoxy-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (70 mg, yield 80%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.79 (s, 3H), 3.82 (s, 3H), 3.93 (s, 6H), 5.11 (bs, 1H), 6.37 (d, J = 5.12 Hz, 1H), 6.66 (d, J = 8.54 Hz, 2H), 6.91 (d, J = 8.54 Hz, 2H), 7.03 (d, J = 8.05 Hz, 1H), 7.35 (s, 1H), 7.43 (s, 1H), 7.49 (s, 1H), 7.55 (d, J = 8.78 Hz, 1H), 8.29 (s, 1H), 8.41 (d, J = 5.37 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 520 (M⁺+1)

Example 1011: N-(2,4-Dichlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}thiourea

[1263] 2,4-Dichloro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-dichloro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2,4-Dichloro-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (78 mg, yield 90%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.11 (s, 3H), 4.17 (s, 3H), 6.79 (d, J = 6.34 Hz, 1H), 7.21 - 7.17 (m, 1H), 7.26 (s, 1H), 7.34 (d, J = 10.25 Hz, 1H), 7.45 - 7.47 (m, 2H), 7.57 (d, J = 1.95 Hz, 1H), 7.60 (s, 1H), 7.79 (d, J = 8.29 Hz, 1H), 7.83 (d, J = 8.29 Hz, 1H), 8.54 (d, J = 6.34 Hz, 1H), 9.44 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 547 (M⁺+1)

Example 1012: N-(2,6-Dichlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}thiourea

[1264] 2,6-Dichloro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,6-dichloro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2,6-Dichloro-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (71 mg, yield 82%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.07 (s, 3H), 4.10 (s, 3H), 6.69 (d, J = 5.86 Hz, 1H), 7.08 - 7.12 (m, 2H), 7.26 - 7.44 (m, 5H), 7.53 (s, 1H), 7.72 (bs, 1H), 8.55 (d, J = 5.85 Hz, 1H), 8.89 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 547 (M⁺+1)

Example 1013: N-(2,4-Difluorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}thiourea

[1265] 2,4-Difluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-difluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2,4-Difluoro-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (66 mg, yield 81%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.11 (s, 3H), 4.14 (s, 3H), 6.74 (d, J = 5.86 Hz, 1H), 6.89 - 6.99 (m, 1H), 7.00 - 7.09 (m, 1H), 7.12 - 7.16 (m, 1H), 7.37 - 7.42 (m, 2H), 7.58 (d, J = 7.56 Hz, 1H), 7.67 (s, 1H), 7.72 (s, 1H), 8.05 - 8.14 (m, 2H), 8.58 (d, J = 6.10 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 514 (M⁺+1)

Example 1014: N-(2,4-Dichlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}thiourea

[1266] 2,4-Dichloro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-dichloro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2,4-Dichloro-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography

on silica gel using chloroform/acetone for development to give the title compound (64 mg, yield 74%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.14 (s, 3H), 4.18 (s, 3H), 6.91 (d, J = 6.83 Hz, 1H), 7.36 (dd, J = 2.07 Hz, 8.42 Hz, 1H), 7.42 - 7.46 (m, 4H), 7.56 - 7.65 (m, 2H), 7.72 (s, 1H), 7.86 (s, 1H), 8.21 (dd, J = 2.44 Hz, J = 11.71 Hz, 1H), 8.66 (d, J = 6.59 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 547 (M⁺+1)

Example 1015: N-(3,5-Dichlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}thiourea

[1267] 3,5-Dichloro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3,5-dichloro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3,5-Dichloro-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (73 mg, yield 84%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.96 (s, 3H), 3.97 (s, 3H), 6.52 (d, J = 5.12 Hz, 1H), 7.43 (s, 2H), 7.51 - 7.55 (m, 2H), 7.59 (m, 1H), 7.95 (s, 1H), 8.00 (s, 1H), 8.05 - 8.78 (m, 1H), 8.53 (d, J = 5.37 Hz, 1H), 11.93 (bs, 1H), 12.42 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 547 (M⁺+1)

Example 1016: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2,4-dimethylbenzoyl)thiourea

[1268] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2,4-dimethylbenzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2,4-dimethyl-1-benzenecarbonyl isothiocyanate was prepared using the resultant 2,4-dimethyl-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 2,4-Dimethyl-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (75 mg, yield 97%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.34 (s, 3H), 2.42 (s, 3H), 3.95 (s, 3H), 3.96 (s, 3H), 6.42 - 6.44 (m, 1H), 7.10 - 7.13 (m, 2H), 7.41 - 7.53 (m, 5H), 7.73 (m, 1H), 8.22 (m, 1H), 8.50 (m, 1H), 11.96 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 523 (M⁺+1)

Example 1017: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2,5-dimethylbenzoyl)thiourea

[1269] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2,5-dimethylbenzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2,5-dimethyl-1-benzenecarbonyl isothiocyanate was prepared using the resultant 2,5-dimethyl-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 2,5-Dimethyl-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (74 mg, yield 94%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.33 (s, 3H), 2.39 (s, 3H), 3.97 (s, 3H), 3.98 (s, 3H), 6.48 (d, J = 5.37 Hz, 1H), 7.14 - 7.27 (m, 2H), 7.35 (s, 1H), 7.43 (s, 1H), 7.50 (d, J = 8.78 Hz, 1H), 7.56 (s, 1H), 7.76 (m, 1H), 8.22 - 8.24 (m, 1H), 8.55 (d, J = 5.37 Hz, 1H), 11.77 (s, 1H), 12.64 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 523 (M⁺+1)

Example 1018: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2,3-dimethylbenzoyl)thiourea

[1270] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2,3-dimethylbenzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2,3-dimethyl-1-benzenecarbonyl isothiocyanate was prepared using the resultant 2,3-dimethyl-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 2,3-Dimethyl-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (76 mg, yield 96%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.29 (s, 6H), 3.94 (s, 3H), 3.96 (s, 3H), 6.57 (d, J = 5.12 Hz, 1H), 7.20 (t, J =

7.45 Hz, 1H), 7.30 - 7.34 (m, 4H), 7.41 (s, 1H), 7.51 (s, 1H), 7.85 - 7.87 (m, 3H), 8.53 (d, J = 5.12 Hz, 1H)
Mass spectrometry value (ESI-MS, m/z): 523 (M⁺+1)

Example 1019: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(3,5-dimethylbenzoyl)thiourea

[1271] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3,5-dimethylbenzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3,5-dimethyl-1-benzenecarbonyl isothiocyanate was prepared using the resultant 3,5-dimethyl-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 3,5-Dimethyl-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (77 mg, yield 97%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.36 (s, 6H), 3.94 (s, 3H), 3.96 (s, 3H), 6.62 (d, J = 5.12 Hz, 1H), 7.31 - 7.32 (m, 2H), 7.41 (s, 1H), 7.52 (s, 1H), 7.64 (s, 2H), 7.84 (m, 2H), 8.53 (d, J = 5.37 Hz, 1H), 11.47 (s, 1H), 12.67 (s, 1H)
Mass spectrometry value (ESI-MS, m/z): 523 (M⁺+1)

Example 1020: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2,6-difluorobenzoyl)thiourea

[1272] 2,6-Difluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,6-difluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2,6-Difluoro-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (59 mg, yield 74%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.94 (s, 3H), 3.96 (s, 3H), 6.57 (d, J = 4.64 Hz, 1H), 7.11 - 7.51 (m, 4H), 7.62 - 7.64 (m, 1H), 7.80 - 7.83 (m, 2H), 8.08 (m, 1H), 8.52 (d, J = 5.12 Hz, 1H), 12.16 (s, 1H), 12.28 (s, 1H)
Mass spectrometry value (ESI-MS, m/z): 530 (M⁺+1)

Example 1021: N-(2,4-Difluorobenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinazolyl)oxy]phenyl]thiourea

[1273] 2,4-Difluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-difluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2,4-Difluoro-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (77 mg, yield 92%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.06 (s, 3H), 4.09 (s, 3H), 6.62 (d, J = 5.61 Hz, 1H), 6.99 - 7.05 (m, 1H), 7.10 - 7.14 (m, 1H), 7.25 - 7.27 (m, 2H), 7.56 (s, 1H), 7.63 (s, 1H), 7.86 (d, J = 8.78 Hz, 2H), 8.15 - 8.21 (m, 1H), 8.52 (d, J = 5.61 Hz, 1H), 9.61 (d, J = 14.64 Hz, 1H)
Mass spectrometry value (ESI-MS, m/z): 497 (M⁺+1)

Example 1022: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2-phenylacetyl)thiourea

[1274] 2-Phenylethanoyl isothiocyanate was prepared using commercially available 2-phenylethanoyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Phenylethanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (64 mg, yield 80%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.82 (s, 2H), 3.96 (s, 3H), 3.98 (s, 3H), 6.51 (d, J = 6.01 Hz, 1H), 7.25 - 7.35 (m, 7H), 7.44 (s, 1H), 7.48 (d, J = 8.78 Hz, 1H), 7.51 (s, 1H), 7.69 (m, 1H), 8.14 - 8.16 (m, 1H), 8.57 (bs, 1H), 11.81 (s, 1H)
Mass spectrometry value (ESI-MS, m/z): 474 (M⁺+1)

Example 1023: N-(2-Cyclohexylacetyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]thiourea

[1275] 2-Cyclohexylethanoyl isothiocyanate was prepared using commercially available 2-cyclohexylethanoyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Cyclohexylethanoyl isothiocyanate

was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (73 mg, yield 90%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.86 - 1.00 (m, 2H), 1.19 - 1.25 (m, 6H), 1.69 (m, 3H), 2.37 (d, J = 6.83 Hz, 2H), 3.96 (s, 3H), 3.99 (s, 3H), 6.67 (m, 1H), 7.34 - 7.36 (m, 2H), 7.44 (s, 1H), 7.59 (s, 1H), 7.81 - 7.84 (m, 2H), 8.63 (m, 1H), 11.48 (s, 1H), 12.41 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 480 (M⁺+1)

Example 1024: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl]-N'-(2-phenylacetyl)thiourea

[1276] 2-Phenylethanoyl isothiocyanate was prepared using commercially available 2-phenylethanoyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Phenylethanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (65 mg, yield 83%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.83 (s, 2H), 3.92 (s, 3H), 3.95 (s, 3H), 6.64 (d, J = 5.12 Hz, 1H), 7.13 (d, J = 9.51 Hz, 1H), 7.29 - 7.36 (m, 6H), 7.41 (s, 1H), 7.46 (s, 1H), 8.05 (t, J = 8.66 Hz, 1H), 8.55 (d, J = 5.12 Hz, 1H), 11.89 (s, 1H), 12.26 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

Example 1025: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-[3-(2-methoxyphenyl)propanoyl]thiourea

[1277] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-(2-methoxyphenyl)propanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-(2-methoxyphenyl)propanoyl isothiocyanate was prepared using the resultant 3-(2-methoxyphenyl)propanoyl chloride as a starting compound according to the description of the literature. 3-(2-Methoxyphenyl)propanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (60 mg, yield 74%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.71 - 2.75 (m, 2H), 2.85 - 2.89 (m, 2H), 3.81 (s, 3H), 3.94 (s, 3H), 3.96 (s, 3H), 6.55 (d, J = 5.12 Hz, 1H), 6.87 (t, J = 7.44 Hz, 1H), 6.95 (d, J = 8.29 Hz, 1H), 7.16 - 7.22 (m, 2H), 7.28 (d, J = 8.54 Hz, 2H), 7.39 (s, 1H), 7.49 (s, 1H), 7.76 - 7.79 (m, 2H), 8.50 (d, J = 6.04 Hz, 1H), 11.49 (s, 1H), 12.59 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 518 (M⁺+1)

Example 1026: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl]-N'-(3-phenylpropanoyl)thiourea

[1278] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-phenylpropanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-phenylpropanoyl isothiocyanate was prepared using the resultant 3-phenylpropanoyl chloride as a starting compound according to the description of the literature. 3-Phenylpropanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (60 mg, yield 74%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.81 - 2.91 (m, 2H), 2.99 - 3.03 (m, 2H), 4.07 (s, 3H), 4.09 (s, 3H), 6.76 (d, J = 6.01 Hz, 1H), 7.06 - 7.11 (m, 2H), 7.21 - 7.32 (m, 3H), 7.56 (s, 3H), 7.73 (bs, 1H), 8.48 (m, 1H), 8.59 (d, J = 5.86 Hz, 1H), 11.49 (s, 1H), 12.74 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 506 (M⁺+1)

Example 1027: N-(3-Cyclopentylpropanoyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl]thiourea

[1279] 3-Cyclopentylpropanoyl isothiocyanate was prepared using commercially available 3-cyclopentylpropanoyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Cyclopentylpropanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature

for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (63 mg, yield 80%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.13 - 1.25 (m, 4H), 1.50 - 1.61 (m, 7H), 1.75 (m, 2H), 3.92 (s, 3H), 3.95 (s, 3H), 6.60 (d, J = 5.12 Hz, 1H), 7.34 (d, J = 11.22 Hz, 1H), 7.28 (m, 1H), 7.32 - 7.35 (m, 1H), 7.41 (s, 1H), 7.45 (s, 1H), 8.11 (m, 1H), 8.53 (d, J = 5.12 Hz, 1H), 11.63 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 498 (M⁺+1)

Example 1028: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]-N'-(3-phenylpropanoyl)thiourea

[1280] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-phenylpropanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-phenylpropanoyl isothiocyanate was prepared using the resultant 3-phenylpropanoyl chloride as a starting compound according to the description of the literature. 3-Phenylpropanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (57 mg, yield 71%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.79 - 2.84 (m, 2H), 2.89 - 2.94 (m, 2H), 4.02 (s, 3H), 4.03 (s, 3H), 6.88 (bs, 1H), 7.21 - 7.33 (m, 6H), 7.59 - 7.61 (m, 3H), 7.72 (s, 1H), 8.13 (d, J = 13.17 Hz, 1H), 11.65 (s, 1H), 12.67 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 506 (M⁺+1)

Example 1029: N-(3-Cyclopentylpropanoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}thiourea

[1281] 3-Cyclopentylpropanoyl isothiocyanate was prepared using commercially available 3-cyclopentylpropanoyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Cyclopentylpropanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (69 mg, yield 88%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.11 (m, 2H), 1.49 - 1.62 (m, 7H), 1.75 - 1.91 (m, 4H), 3.95 (s, 3H), 3.96 (s, 3H), 6.52 (d, J = 5.37 Hz, 1H), 7.43 (s, 1H), 7.47 - 7.56 (m, 3H), 8.05 (d, J = 4.39 Hz, 1H), 8.52 (d, J = 5.12 Hz, 1H), 11.58 (s, 1H), 12.66 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 498 (M⁺+1)

Example 1030: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(3-cyclopentylpropanoyl)thiourea

[1282] 3-Cyclopentylpropanoyl isothiocyanate was prepared using commercially available 3-cyclopentylpropanoyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Cyclopentylpropanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (68 mg, yield 88%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.07 (m, 4H), 1.48 - 1.71 (m, 9H), 4.05 (s, 3H), 4.07 (s, 3H), 6.88 (d, J = 6.83 Hz, 1H), 7.55 (s, 1H), 7.65 (d, J = 9.03 Hz, 1H), 7.78 - 7.81 (m, 2H), 8.26 - 8.28 (m, 1H), 8.87 (d, J = 6.59 Hz, 1H), 11.61 (s, 1H), 12.66 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 515 (M⁺+1)

Example 1031: N-[2-(Benzyloxy)acetyl]-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}thiourea

[1283] 2-(Benzyloxy)ethanoyl isothiocyanate was prepared using commercially available 2-(benzyloxy)ethanoyl chloride (80 mg) as a starting compound according to the description of the literature. 2-(Benzyloxy)ethanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (38 mg, yield 43%).

Mass spectrometry value (ESI-MS, m/z): 522 (M⁺+1)

Example 1032: N-[2-(Benzyloxy)acetyl]-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}thiourea

[1284] 2-(Benzyloxy)ethanoyl isothiocyanate was prepared using commercially available 2-(benzyloxy)ethanoyl chloride (80 mg) as a starting compound according to the description of the literature. 2-(Benzyloxy)ethanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution; and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (33 mg, yield 40%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.96 (s, 6H), 4.13 (s, 2H), 4.64 (s, 2H), 6.48 (d, J = 5.37 Hz, 2H), 7.32 - 7.45 (m, 6H), 7.54 (m, 2H), 7.90 - 7.94 (m, 2H), 8.50 (d, J = 5.12 Hz, 1H), 10.15 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 522 (M⁺+1)

Example 1033: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-furancarboxyl)thiourea

[1285] 2-Furancarboxyl isothiocyanate was prepared using commercially available 2-furancarboxyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Furancarboxyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (40 mg, yield 53%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.94 (s, 3H), 3.96 (s, 3H), 6.56 (d, J = 5.12 Hz, 1H), 6.73 - 6.77 (m, 2H), 7.32 (d, J = 8.78 Hz, 1H), 7.41 (s, 1H), 7.51 - 7.52 (m, 2H), 7.79 (d, J = 8.78 Hz, 1H), 7.86 (m, 1H), 8.01 (s, 2H), 8.08 (s, 1H), 8.51 (d, J = 4.88, 1H)

Mass spectrometry value (ESI-MS, m/z): 450 (M⁺+1)

Example 1034: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(3-thienylcarbonyl)thiourea

[1286] 3-Thiophenecarbonyl isothiocyanate was prepared using commercially available 3-thiophenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Thiophenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (45 mg, yield 68%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.93 (s, 3H), 3.95 (s, 3H), 6.55 (d, J = 5.37 Hz, 1H), 7.26 (t, J = 4.27 Hz, 1H), 7.31 (d, J = 9.03 Hz, 2H), 7.41 (s, 1H), 7.50 (s, 1H), 7.81 (d, J = 9.03 Hz, 2H), 8.05 (d, J = 4.88 Hz, 1H), 8.41 (d, J = 3.90 Hz, 1H), 8.51 (d, J = 5.12 Hz, 1H), 11.65 (s, 1H), 12.49 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 466 (M⁺+1)

Example 1035: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-(2-furancarboxyl)thiourea

[1287] 2-Furancarboxyl isothiocyanate was prepared using commercially available 2-furancarboxyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Furancarboxyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (47 mg, yield 68%).

Mass spectrometry value (ESI-MS, m/z) : 468 (M⁺+1)

Example 1036: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-(3-thienylcarbonyl)thiourea

[1288] 3-Thiophenecarbonyl isothiocyanate was prepared using commercially available 3-thiophenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Thiophenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (45 mg, yield 58%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.93 (s, 3H), 3.96 (s, 3H), 6.67 (d, J = 5.12 Hz, 1H), 7.15 - 7.18 (m, 1H), 7.26 - 7.28 (m, 2H), 7.39 - 7.43 (m, 2H), 7.48 (s, 1H), 7.99 - 8.08 (m, 2H), 8.42 (d, J = 3.42 Hz, 1H), 8.57 (d, J = 5.12 Hz,

1H), 10.01 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 484 (M⁺+1)

Example 1037: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl]-N'-(2,5-dimethyl-3-furyl)carbonyl]thiourea

[1289] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2,5-dimethyl-3-furoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2,5-dimethyl-3-furancarbonyl isothiocyanate was prepared using the resultant 2,5-dimethyl-3-furancarbonyl chloride as a starting compound according to the description of the literature. 2,5-Dimethyl-3-furancarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (38 mg, yield 48%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.26 (s, 3H), 2.55 (s, 3H), 3.92 (s, 3H), 3.95 (s, 3H), 6.65 (d, J = 5.37 Hz, 1H), 6.89 (s, 1H), 7.13 - 7.14 (m, 1H), 7.34 - 7.37 (m, 1H), 7.41 (s, 1H), 7.46 (s, 1H), 8.05 - 8.07 (m, 1H), 8.54 (d, J = 5.15 Hz, 1H), 11.13 (s, 1H), 12.61 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 496 (M⁺+1)

Example 1038: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl]-N'-(3-methyl-2-thienyl)carbonyl]thiourea

[1290] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-methyl-2-thiophenecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-methyl-2-thiophenecarbonyl isothiocyanate was prepared using the resultant 3-methyl-2-thiophenecarbonyl chloride as a starting compound according to the description of the literature. 3-Methyl-2-thiophenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (42 mg, yield 53%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.51 (s, 3H), 3.92 (s, 3H), 3.96 (s, 3H), 6.66 (d, J = 5.12 Hz, 1H), 7.09 (d, J = 4.88 Hz, 1H), 7.14 - 7.16 (m, 1H), 7.38 (dd, J = 2.56 Hz, 11.01 Hz, 1H), 7.42 (s, 1H), 7.46 (s, 1H), 7.86 (d, J = 4.88 Hz, 1H), 8.07 (t, J = 8.54 Hz, 1H), 8.55 (d, J = 5.37 Hz, 1H), 11.25 (s, 1H), 12.22 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 498 (M⁺+1)

Example 1039: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]-N'-(2,5-dimethyl-3-furyl)carbonyl]thiourea

[1291] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2,5-dimethyl-3-furoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2,5-dimethyl-3-furancarbonyl isothiocyanate was prepared using the resultant 2,5-dimethyl-3-furancarbonyl chloride as a starting compound according to the description of the literature. 2,5-Dimethyl-3-furancarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (51 mg, yield 64%).

¹H-NMR (DMSO-d₆, 400 MHz) : δ 2.26 (s, 3H), 2.55 (s, 3H), 3.96 (s, 6H), 6.51 (d, J = 5.37 Hz, 1H), 6.87 (s, 1H), 7.42 (s, 1H), 7.47 - 7.59 (m, 3H), 8.07 (d, J = 10.25 Hz, 1H), 8.51 (d, J = 5.12 Hz, 1H), 11.02 (s, 1H), 12.81 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 496 (M⁺+1)

Example 1040: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]-N'-(5-methyl-2-thienyl)carbonyl]thiourea

[1292] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 5-methyl-2-thiophenecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 5-methyl-2-thiophenecarbonyl isothiocyanate was prepared using the resultant 5-methyl-2-thiophenecarbonyl chloride as a starting compound according to the description of the literature. 5-Methyl-2-thiophenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (49 mg, yield 62%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.58 (s, 3H), 4.07 (s, 3H), 4.09 (s, 3H), 6.62 (d, J = 5.61 Hz, 1H), 7.25 - 7.27 (m,

1H), 7.32 - 7.35 (m, 1H), 7.46 - 7.50 (m, 1H), 7.57 - 7.58 (m, 2H), 7.63 (s, 1H), 7.88 - 7.90 (m, 2H), 8.53 (d, J = 5.61 Hz, 1H), 8.86 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 498 (M⁺+1)

5 Example 1041: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-[[diethylamino]carbonyl]amino}methanethioamide

[1293] (Diethylamino)methanoyl isothiocyanate was prepared using commercially available N,N-diethylcarbamic chloride (80 mg) as a starting compound according to the description of the literature. (Diethylamino)methanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (42 mg, yield 55%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.26 - 1.29 (m, 6H), 3.93 (s, 3H), 3.95 (s, 3H), 4.22 - 4.24 (m, 4H), 6.54 (d, J = 5.12 Hz, 1H), 7.11 (m, 2H), 7.29 - 7.31 (m, 2H), 7.41 (s, 1H), 7.50 (s, 1H), 7.73 (m, 2H), 8.52 (d, J = 5.12 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 455 (M⁺+1)

Example 1042: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-[[di(2-chloroethyl)amino]carbonyl]amino}methanethioamide

[1294] [Di(2-chloroethyl)amino]methanoyl isothiocyanate was prepared using commercially available N,N-di(2-chloroethyl)carbamic chloride (80 mg) as a starting compound according to the description of the literature. [Di(2-chloroethyl)amino]methanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (48 mg, yield 55%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.57 - 3.62 (m, 4H), 3.80 - 3.82 (m, 2H), 3.95 (s, 3H), 3.97 (s, 3H), 4.11 - 4.13 (m, 2H), 7.55 (m, 1H), 7.29 - 7.31 (m, 2H), 7.42 (s, 1H), 7.55 (s, 1H), 7.73 - 7.75 (m, 3H), 8.57 (d, J = 5.37 Hz, 1H), 12.25 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 524 (M⁺+1)

Example 1043: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-[[diisopropylamino]carbonyl]amino}methanethioamide

[1295] (Diisopropylamino)methanoyl isothiocyanate was prepared using commercially available N,N-diisopropylcarbamic chloride (80 mg) as a starting compound according to the description of the literature. (Diisopropylamino)methanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (50 mg, yield 62%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.19 (d, J = 6.10 Hz, 2H), 1.27 (d, J = 6.83 Hz, 12H), 3.94 (s, 3H), 3.96 (s, 3H), 6.39 (d, J = 5.12 Hz, 1H), 7.42 - 7.46 (m, 4H), 7.53 (s, 2H), 7.64 (m, 1H), 8.13 (m, 1H), 8.49 (d, J = 4.88 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 483 (M⁺+1)

Example 1044: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-tetrahydro-1H-1-pyrrolylcarbonylthiourea

[1296] 1-Pyrrolidinecarbonyl isothiocyanate was prepared using commercially available 1-pyrrolidinecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 1-Pyrrolidinecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (48 mg, yield 63%).

¹H-NMR (DMSO-d₆, 400 MHz) : δ 1.85 (m, 8H), 3.92 (s, 3H), 3.94 (s, 3H), 6.52 (d, J = 4.88 Hz, 1H), 7.27 (d, J = 7.81 Hz, 2H), 7.39 (s, 1H), 7.49 (s, 1H), 7.75 (m, 2H), 8.49 (d, J = 5.13 Hz, 1H), 9.59 (s, 1H), 12.80 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 453 (M⁺+1)

Example 1045: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-morpholinocarbonylthiourea

[1297] 4-Morpholinecarbonyl isothiocyanate was prepared using commercially available 4-morpholinecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-Morpholinecarbonyl isothiocyanate

was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (49 mg, yield 62%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.53 - 3.55 (m, 4H), 3.74 - 3.78 (m, 4H), 4.05 (s, 3H), 4.07 (s, 3H), 6.58 (d, J = 5.61 Hz, 1H), 7.21 (d, J = 8.78 Hz, 2H), 7.26 (s, 1H), 7.54 (d, J = 4.88 Hz, 2H), 7.76 (d, J = 9.03 Hz, 2H), 7.98 (bs, 1H), 8.51 (d, J = 5.37 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 469 (M⁺+1)

Example 1046: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-{[(methylanilino)carbonyl]amino}methanethioamide

[1298] (Methylanilino)methanoyl isothiocyanate was prepared using commercially available N-methyl-N-phenylcarbamic chloride (80 mg) as a starting compound according to the description of the literature. (Methylanilino)methanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (52 mg, yield 63%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.57 (bs, 3H), 3.93 (s, 3H), 3.94 (s, 3H), 6.43 (d, J = 5.37 Hz, 1H), 7.13 - 7.16 (m, 2H), 7.26 - 7.28 (m, 1H), 7.34 - 7.45 (m, 6H), 7.51 (s, 1H), 7.57 (d, J = 9.03 Hz, 2H), 8.31 (s, 1H), 8.46 (d, J = 5.37 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 489 (M⁺+1)

Example 1047: N-[10,11-Dihydro-5H-dibenzo(b,f)-azepin-5-ylcarbonyl]-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1299] 10,11-Dihydro-5H-dibenzo(b,f)azepine-5-carbonyl isothiocyanate was prepared using commercially available 10,11-dihydro-5H-dibenzo(b,f)azepine-5-carbonyl chloride (80 mg) as a starting compound according to the description of the literature. 10,11-Dihydro-5H-dibenzo(b,f)azepine-5-carbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (61 mg, yield 65%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.86 (m, 2H), 1.25 (m, 2H), 3.94 (s, 3H), 3.95 (s, 3H), 6.49 (d, J = 5.37 Hz, 1H), 7.35 - 7.56 (m, 12H), 8.02 (m, 1H), 8.49 - 8.51 (m, 2H), 12.36 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 595 (M⁺+1)

Example 1048: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-{[(diethylamino)carbonyl]amino}methanethioamide

[1300] (Diethylamino)methanoyl isothiocyanate was prepared using commercially available N,N-diethylcarbamic chloride (80 mg) as a starting compound according to the description of the literature. (Diethylamino)methanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (52 mg, yield 38%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.29 (t, J = 7.19 Hz, 6H), 3.95 (s, 6H), 4.23 - 4.25 (m, 4H), 6.39 (d, J = 5.12 Hz, 1H), 7.41 (s, 1H), 7.45 (d, J = 8.78 Hz, 1H), 7.52 (s, 1H), 7.65 (m, 2H), 8.09 (m, 1H), 8.49 (d, J = 5.61 Hz, 1H), 11.37 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 489 (M⁺+1)

Example 1049: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-{[di(2-chloroethyl)amino]carbonyl}amino}methanethioamide

[1301] [Di(2-chloroethyl)amino]methanoyl isothiocyanate was prepared using commercially available N,N-di(2-chloroethyl)carbamic chloride (80 mg) as a starting compound according to the description of the literature. [Di(2-chloroethyl)amino]methanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chroma-

tography on silica gel using chloroform/acetone for development to give the title compound (51 mg, yield 60%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.55 - 3.63 (m, 4H), 3.81 - 3.84 (m, 2H), 3.95 (s, 6H), 4.11 - 4.15 (m, 2H), 6.41 (d, J = 5.12 Hz, 1H), 7.40 - 7.44 (m, 3H), 7.52 (s, 1H), 7.61 - 7.63 (m, 1H), 8.09 - 8.12 (m, 1H), 8.49 (d, J = 5.12 Hz, 1H), 12.29 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 558 (M⁺+1)

Example 1050: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-{[(diisopropylamino)carbonyl]amino}methanethioamide

[1302] (Diisopropylamino)methanoyl isothiocyanate was prepared using commercially available N,N-diisopropylcarbamic chloride (80 mg) as a starting compound according to the description of the literature. (Diisopropylamino)methanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (49 mg, yield 63%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.18 (d, J = 6.01 Hz, 2H), 1.27 (d, J = 6.83 Hz, 12H), 3.93 (s, 3H), 3.95 (s, 3H), 6.53 (d, J = 5.12 Hz, 1H), 7.28 (d, J = 8.78 Hz, 2H), 7.41 (s, 1H), 7.50 (s, 1H), 7.73 - 7.75 (m, 3H), 8.51 (d, J = 5.12 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 518 (M⁺+1)

Example 1051: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-tetrahydro-1H-1-pyrrolylcarbonylthiourea

[1303] 1-Pyrrolidinecarbonyl isothiocyanate was prepared using commercially available 1-pyrrolidinecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 1-Pyrrolidinecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (52 mg, yield 70%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.85 - 1.99 (m, 8H), 3.95 (s, 6H), 6.41 (d, J = 5.37 Hz, 1H), 7.42 (s, 1H), 7.46 (d, J = 8.54 Hz, 1H), 7.53 (s, 1H), 7.64 - 7.66 (m, 2H), 8.17 - 8.19 (m, 2H), 8.50 (d, J = 5.37 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 487 (M⁺+1)

Example 1052: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-morpholinocarbonylthiourea

[1304] 4-Morpholinecarbonyl isothiocyanate was prepared using commercially available 4-morpholinecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-Morpholinecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (40 mg, yield 52%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.53 - 3.56 (m, 4H), 3.75 - 3.77 (m, 4H), 4.08 (s, 3H), 4.10 (s, 3H), 5.77 (bs, 1H), 6.49 (d, J = 5.61 Hz, 1H), 7.26 - 7.29 (m, 1H), 7.63 (s, 1H), 7.68 - 7.70 (m, 2H), 8.01 (s, 1H), 8.04 (d, J = 2.44 Hz, 1H), 8.52 (d, J = 5.85 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 503 (M⁺+1)

Example 1053: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-{[(methylanilino)carbonyl]amino}methanethioamide

[1305] (Methylanilino)methanoyl isothiocyanate was prepared using commercially available N-methyl-N-phenylcarbamic chloride (80 mg) as a starting compound according to the description of the literature. (Methylanilino)methanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (56 mg, yield 71%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.57 (bs, 3H), 3.94 (s, 6H), 6.32 (d, J = 5.12 Hz, 1H), 7.28 - 7.44 (m, 8H), 7.52 - 7.58 (m, 2H), 7.56 (s, 1H), 8.46 - 8.48 (m, 2H)

Mass spectrometry value (ESI-MS, m/z): 524 (M⁺+1)

Example 1054: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[10,11-dihydro-5H-dibenzo(b,f)azepin-5-ylcarbonyl]thiourea

[1306] 10,11-Dihydro-5H-dibenzo(b,f)azepine-5-carbonyl isothiocyanate was prepared using commercially available 10,11-dihydro-5H-dibenzo(b,f)-azepine-5-carbonyl chloride (80 mg) as a starting compound according to the description of the literature. 10,11-Dihydro-5H-dibenzo(b,f)azepine-5-carbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (46 mg, yield 50%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.86 (m, 2H), 1.25 (m, 2H), 3.94 (s, 3H), 3.95 (s, 3H), 6.39 (d, J = 5.12 Hz, 1H), 7.35 (m, 6H), 7.41 (s, 1H), 7.45 (d, J = 8.78 Hz, 1H), 7.51 (s, 1H), 7.56 - 7.57 (m, 2H), 7.68 (dd, J = 2.44 Hz, 9.03 Hz, 1H), 8.14 (s, 1H), 8.49 (d, J = 5.12 Hz, 1H), 8.53 (s, 1H), 12.29 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 612 (M⁺+1)

Example 1055: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-[(2-phenylcyclopropyl)carbonyl]thiourea

[1307] 2-Phenyl-1-cyclopropanecarbonyl isothiocyanate was prepared using commercially available 2-phenyl-1-cyclopropanecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Phenyl-1-cyclopropanecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (53 mg, yield 63%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.09 (m, 1H), 1.52 (m, 2H), 1.59 (m, 2H), 3.94 (s, 3H), 3.96 (s, 3H), 6.59 (d, J = 5.37 Hz, 1H), 7.19 - 7.32 (m, 5H), 7.41 (m, 2H), 7.52 (m, 2H), 7.78 - 7.80 (m, 3H), 8.54 (m, 1H)

Mass spectrometry value (ESI-MS, m/z): 500 (M⁺+1)

Example 1056: N-Cyclopropylcarbonyl-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]thiourea

[1308] 1-Cyclopropanecarbonyl isothiocyanate was prepared using commercially available 1-cyclopropanecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 1-Cyclopropanecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (46 mg, yield 66%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.96 - 0.99 (m, 4H), 2.08 - 2.13 (m, 2H), 3.95 (s, 6H), 6.72 (d, J = 5.12 Hz, 1H), 7.41 (s, 1H), 7.45 - 7.52 (m, 2H), 8.04 (d, J = 11.95 Hz, 1H), 8.50 (d, J = 5.12 Hz, 1H), 11.89 (s, 1H), 12.64 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 442 (M⁺+1)

Example 1057: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]-N'-[(2-phenylcyclopropyl)carbonyl]thiourea

[1309] 2-Phenyl-1-cyclopropanecarbonyl isothiocyanate was prepared using commercially available 2-phenyl-1-cyclopropanecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Phenyl-1-cyclopropanecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (51 mg, yield 62%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.08 - 1.25 (m, 1H), 1.53 (m, 2H), 1.59 - 1.62 (m, 2H), 3.95 (s, 6H), 6.49 (d, J = 5.12 Hz, 1H), 7.19 - 7.55 (m, 8H), 8.05 (d, J = 10.00 Hz, 1H), 8.50 (d, J = 5.37 Hz, 1H), 11.88 (s, 1H), 12.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 518 (M⁺+1)

Example 1058: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-cyclopropylcarbonylthiourea

[1310] 1-Cyclopropanecarbonyl isothiocyanate was prepared using commercially available 1-cyclopropanecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 1-Cyclopropanecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using

chloroform/acetone for development to give the title compound (36 mg, yield 52%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.93 - 0.99 (m, 4H), 2.12 (m, 2H), 3.94 (s, 3H), 3.96 (s, 3H), 6.41 (d, J = 5.37 Hz, 1H), 7.33 (d, J = 11.95 Hz, 1H), 7.41 (s, 1H), 7.45 (d, J = 8.78 Hz, 1H), 7.52 (s, 1H), 7.64 - 7.67 (m, 1H), 8.14 (s, 1H), 8.49 (d, J = 5.37 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 458 (M⁺+1)

Example 1059: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-[(2-phenylcyclopropyl)carbonyl]thiourea

[1311] 2-Phenyl-1-cyclopropanecarbonyl isothiocyanate was prepared using commercially available 2-phenyl-1-cyclopropanecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Phenyl-1-cyclopropanecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (48 mg, yield 60%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.09 - 1.11 (m, 1H), 1.53 (m, 2H), 1.60 (m, 2H), 3.94 (s, 3H), 3.96 (s, 3H), 6.40 (d, J = 5.37 Hz, 1H), 7.16 - 7.34 (m, 5H), 7.41 (s, 1H), 7.45 (d, J = 8.78 Hz, 1H), 7.52 (s, 1H), 7.67 (dd, J = 2.32 Hz, 8.91 Hz, 1H), 8.14 (d, J = 2.44 Hz, 1H), 8.49 (d, J = 5.12 Hz, 1H), 11.88 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 535 (M⁺+1)

Example 1060: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[(2-phenylcyclopropyl)carbonyl]thiourea

[1312] 2-Phenyl-1-cyclopropanecarbonyl isothiocyanate was prepared using commercially available 2-phenyl-1-cyclopropanecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Phenyl-1-cyclopropanecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (50 mg, yield 60%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.93 - 0.97 (m, 1H), 1.31 (m, 1H), 1.52 - 1.60 (m, 2H), 3.98 (s, 6H), 6.55 (d, J = 5.61 Hz, 1H), 7.18 - 7.33 (m, 5H), 7.45 (s, 1H), 7.56 (d, J = 8.54 Hz, 1H), 7.59 (s, 1H), 7.69 (m, 1H), 8.17 - 8.19 (m, 1H), 8.60 (d, J = 5.91 Hz, 1H), 11.88 (s, 1H), 12.59 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 501 (M⁺+1)

Example 1061: N-Cyclopentylcarbonyl-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1313] 1-Cyclopentanecarbonyl isothiocyanate was prepared using commercially available 1-cyclopentanecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 1-Cyclopentanecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (43 mg, yield 57%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.85 - 0.88 (m, 1H), 1.08 - 1.11 (m, 1H), 1.24 (bs, 1H), 1.57 - 1.91 (m, 6H), 3.93 (s, 3H), 3.95 (s, 3H), 6.54 (d, J = 5.37 Hz, 1H), 7.19 (d, J = 8.78 Hz, 1H), 7.29 (d, J = 8.78 Hz, 2H), 7.39 (d, J = 7.81 Hz, 1H), 7.50 (d, J = 5.61 Hz, 1H), 7.73 - 7.78 (m, 3H), 8.51 (d, J = 5.37 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 452 (M⁺+1)

Example 1062: N-Cyclohexylcarbonyl-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1314] 1-Cyclohexanecarbonyl isothiocyanate was prepared using commercially available 1-cyclohexanecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 1-Cyclohexanecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (60 mg, yield 47%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.21 - 1.38 (m, 6H), 1.66 - 1.85 (m, 5H), 3.92 (s, 3H), 3.95 (s, 3H), 6.54 (d, J = 5.12 Hz, 1H), 7.28 (d, J = 9.03 Hz, 3H), 7.39 (s, 1H), 7.49 (s, 1H), 7.76 (d, J = 8.78 Hz, 1H), 8.50 (d, J = 5.12 Hz, 1H), 11.41 (bs, 1H), 12.56 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 466 (M⁺+1)

Example 1063: N-Cyclopentylcarbonyl-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}thiourea

[1315] 1-Cyclopentanecarbonyl isothiocyanate was prepared using commercially available 1-cyclopentanecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 1-Cyclopentanecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (35 mg, yield 47%).

¹H-NMR (CDCl₃, 400 MHz): δ 0.879 (m, 1H), 1.08 (m, 1H), 1.17 (m, 1H), 1.63 - 1.97 (m, 6H), 4.07 (s, 3H), 4.09 (s, 3H), 6.86 (d, J = 6.01 Hz, 1H), 7.16 (dd, J = 9.52 Hz, 22.93 Hz, 1H), 7.63 (s, 1H), 7.69 (s, 2H), 8.56 (m, 1H), 8.68 (d, J = 6.34 Hz, 1H), 11.47 (bs, 1H), 12.88 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 470 (M⁺+1)

Example 1064: N-Cyclohexylcarbonyl-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}thiourea

[1316] 1-Cyclohexanecarbonyl isothiocyanate was prepared using commercially available 1-cyclohexanecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 1-Cyclohexanecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (47 mg, yield 61%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.21 - 1.39 (m, 6H), 1.66 - 1.90 (m, 5H), 3.92 (s, 3H), 3.95 (s, 3H), 6.64 (d, J = 5.12 Hz, 1H), 7.12 (d, J = 8.78 Hz, 1H), 7.35 (dd, J = 2.55 Hz, 11.10 Hz, 1H), 7.41 (s, 1H), 7.45 (s, 1H), 8.09 (t, J = 8.79 Hz, 1H), 8.53 (d, J = 5.37 Hz, 1H), 11.57 (s, 1H), 12.42 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 484 (M⁺+1)

Example 1065: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(3-ethoxypropanoyl)thiourea

[1317] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-ethoxypropanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-ethoxypropanoyl isothiocyanate was prepared using the resultant 3-ethoxypropanoyl chloride as a starting compound according to the description of the literature. 3-Ethoxypropanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (55 mg, yield 72%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.92 - 0.95 (m, 3H), 2.74 (m, 2H), 3.44 - 3.46 (m, 2H), 3.64 - 3.65 (m, 2H), 3.95 (s, 3H), 3.96 (s, 3H), 6.44 (d, J = 5.37 Hz, 1H), 7.43 (s, 1H), 7.49 (d, J = 8.78 Hz, 2H), 7.54 (s, 1H), 7.70 (m, 1H), 8.16 (m, 1H), 8.53 (d, J = 5.12 Hz, 1H), 11.71 (s, 1H), 12.32 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 456 (M⁺+1)

Example 1066: N-(4-Chlorobutanoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}thiourea

[1318] 4-Chlorobutanoyl isothiocyanate was prepared using commercially available 4-chlorobutanoyl chloride (80 mg) as a starting compound according to the description of the literature. 4-Chlorobutanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (51 mg, yield 67%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.02 - 2.05 (m, 2H), 2.63 - 2.67 (m, 2H), 3.67 - 3.70 (m, 2H), 3.93 (s, 3H), 3.96 (s, 3H), 6.66 (d, J = 5.37 Hz, 1H), 7.14 (d, J = 6.59 Hz, 1H), 7.36 - 7.38 (m, 1H), 7.42 (s, 1H), 7.47 (s, 1H), 8.08 (t, J = 8.78 Hz, 1H), 8.56 (d, J = 5.37 Hz, 1H), 11.71 (s, 1H), 12.32 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 479 (M⁺+1)

Example 1067: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-[3-(methylsulfanyl)propanoyl]thiourea

[1319] 3-(Methylsulfanyl)propanoyl isothiocyanate was prepared using commercially available 3-(methylsulfanyl)propanoyl chloride (80 mg) as a starting compound according to the description of the literature. 3-(Methylsulfanyl)

propanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (43 mg, yield 57%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.74 - 2.76 (m, 2H), 2.79 - 2.81 (m, 2H), 3.17 (s, 3H), 3.92 (s, 3H), 3.96 (s, 3H), 6.65 (d, J = 5.12 Hz, 1H), 7.14 (d, J = 9.27 Hz, 1H), 7.35 - 7.38 (m, 1H), 7.42 (s, 1H), 7.46 (s, 1H), 8.08 (t, J = 8.90 Hz, 1H), 8.55 (d, J = 5.12 Hz, 1H), 11.71 (s, 1H), 12.34 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 476 (M⁺+1)

Example 1068: N-(4-Chlorobutanoyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]thiourea

[1320] 4-Chlorobutanoyl isothiocyanate was prepared using commercially available 4-chlorobutanoyl chloride (80 mg) as a starting compound according to the description of the literature. 4-Chlorobutanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-3-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (41 mg, yield 54%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.02 - 2.06 (m, 2H), 2.63 - 2.67 (m, 2H), 3.68 - 3.71 (m, 2H), 3.97 (s, 3H), 3.98 (s, 3H), 6.63 (d, J = 5.61 Hz, 1H), 7.44 - 7.59 (m, 6H), 8.07 (d, J = 11.95 Hz, 1H), 8.59 (d, J = 5.61 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 478 (M⁺+1)

Example 1069: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]-N'-[3-(methylsulfanyl)propanoyl]thiourea

[1321] 3-(Methylsulfanyl)propanoyl isothiocyanate was prepared using commercially available 3-(methylsulfanyl)propanoyl chloride (80 mg) as a starting compound according to the description of the literature. 3-(Methylsulfanyl)propanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-3-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (38 mg, yield 50%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.54 (s, 3H), 2.74 - 2.81 (m, 4H), 3.95 (s, 6H), 6.51 (d, J = 5.12 Hz, 1H), 7.41 (s, 1H), 7.48 - 7.53 (m, 3H), 8.04 (d, J = 10.49 Hz, 1H), 8.50 (d, J = 5.12 Hz, 1H), 11.64 (s, 1H), 12.59 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 476 (M⁺+1)

Example 1070: N-(3,4-Dimethoxybenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]thiourea

[1322] 3,4-Dimethoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3,4-dimethoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3,4-dimethoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (54 mg, yield 63%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.79 (s, 3H), 3.81 (s, 3H), 3.96 (s, 3H), 5.47 (bs, 1H), 6.38 (bs, 1H), 6.44 - 6.47 (m, 1H), 6.54 (dd, J = 2.52 Hz, J = 14.79 Hz, 1H), 7.02 - 7.08 (m, 3H), 7.37 (s, 1H), 7.43 (s, 2H), 7.49 (s, 1H), 7.53 - 7.57 (m, 2H), 8.46 (d, J = 5.12 Hz, 1H), 12.64 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 538 (M⁺+1)

Example 1071: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(3-ethoxypropanoyl)thiourea

[1323] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-ethoxypropanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-ethoxypropanoyl isothiocyanate was prepared using the resultant 3-ethoxypropanoyl chloride as a starting compound according to the description of the literature. 3-Ethoxypropanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (46 mg, yield 62%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.06 - 1.13 (m, 3H), 2.72 - 2.75 (m, 2H), 3.44 - 3.47 (m, 2H), 3.64 - 3.67 (m,

2H), 3.95 (s, 3H), 3.97 (s, 3H), 6.63 (d, J = 5.37 Hz, 1H), 7.29 (d, J = 8.54 Hz, 2H), 7.44 (s, 1H), 7.56 (s, 1H), 7.78 - 7.82 (m, 2H), 8.59 (d, J = 5.61 Hz, 1H), 11.51 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 490 (M⁺+1)

5 Example 1072: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-dodecanoylthiourea

[1324] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available dodecanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and dodecanoyl isothiocyanate was prepared using the resultant dodecanoyl chloride as a starting compound according to the description of the literature. Dodecanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (58 mg, yield 60%).

¹H-NMR (CDCl₃, 400 MHz): δ 0.87 - 0.89 (m, 3H), 1.27 (m, 14H), 1.71 - 1.72 (m, 2H), 2.39 - 2.43 (m, 2H), 3.49 (s, 2H), 4.06 (s, 3H), 4.08 (s, 3H), 6.59 (d, J = 5.61 Hz, 1H), 7.21 - 7.26 (m, 4H), 7.55 (s, 1H), 7.59 (s, 1H), 7.79 (d, J = 8.98 Hz, 1H), 8.52 (d, J = 5.61 Hz, 1H), 8.66 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 538 (M⁺+1)

20 Example 1073: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-phenyl}-N'-tetradecanoylthiourea

[1325] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available tetradecanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and tetradecanoyl isothiocyanate was prepared using the resultant tetradecanoyl chloride as a starting compound according to the description of the literature. Tetradecanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (58 mg, yield 60%).

¹H-NMR (CDCl₃, 400 MHz): δ 0.87 - 0.90 (m, 3H), 1.27 (m, 20H), 1.73 (m, 2H), 2.40 - 2.44 (m, 2H), 4.08 (s, 3H), 4.12 (s, 3H), 5.29 (s, 1H), 6.65 (d, J = 6.09 Hz, 1H), 7.23 - 7.26 (m, 2H), 7.58 (s, 1H), 7.83 - 7.85 (m, 3H), 8.52 (d, J = 6.09 Hz, 1H), 8.63 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 566 (M⁺+1)

Example 1074: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-methylhexanoyl)thiourea

[1326] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-methylhexanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-methylhexanoyl isothiocyanate was prepared using the resultant 2-methylhexanoyl chloride as a starting compound according to the description of the literature. 2-Methylhexanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (54 mg, yield 68%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.86 - 0.89 (m, 4H), 1.10 (d, J = 6.83 Hz, 3H), 1.27 - 1.32 (m, 5H), 2.74 - 2.76 (m, 1H), 3.94 (s, 3H), 3.96 (s, 3H), 6.58 (d, J = 5.97 Hz, 1H), 7.31 (d, J = 8.78 Hz, 2H), 7.42 (s, 1H), 7.52 (s, 1H), 7.78 - 7.82 (m, 3H), 8.55 (d, J = 5.37 Hz, 1H), 11.50 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 468 (M⁺+1)

Example 1075: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}-N'-dodecanoylthiourea

[1327] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available dodecanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and dodecanoyl isothiocyanate was prepared using the resultant dodecanoyl chloride as a starting compound according to the description of the literature. Dodecanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (60 mg, yield 68%).

¹H-NMR (CDCl₃, 400 MHz): δ 0.86 - 0.89 (m, 6H), 1.26 - 1.27 (m, 6H), 1.56 - 1.64 (m, 11H), 4.09 (s, 3H), 4.17 (s, 3H), 6.78 (d, J = 6.34 Hz, 1H), 7.08 - 7.13 (m, 2H), 7.26 (s, 1H), 7.59 (s, 1H), 8.12 (bs, 1H), 8.56 (d, J = 6.34 Hz,

1H), 8.62 (m, 1H), 8.79 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 556 (M⁺+1)

Example 1076: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluorophenyl]-N'-tetradecanoylthiourea

[1328] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available tetradecanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and tetradecanoyl isothiocyanate was prepared using the resultant tetradecanoyl chloride as a starting compound according to the description of the literature. Tetradecanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (58 mg, yield 63%).

¹H-NMR (CDCl₃, 400 MHz): δ 0.86 - 0.89 (m, 3H), 1.27 (m, 18H), 2.49 (m, 2H), 2.58 - 2.59 (m, 4H), 4.11 (s, 3H), 4.17 (s, 3H), 6.38 (m, 1H), 7.08 - 7.11 (m, 2H), 7.35 (s, 3H), 7.61 - 7.63 (m, 2H), 8.17 (m, 1H)

Mass spectrometry value (ESI-MS, m/z) : 584 (M⁺+1)

Example 1077: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-[2-methylhexanoyl]thiourea

[1329] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-methylhexanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-methylhexanoyl isothiocyanate was prepared using the resultant 2-methylhexanoyl chloride as a starting compound according to the description of the literature. 2-Methylhexanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (44 mg, yield 58%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.84 - 0.94 (m, 5H), 1.03 - 1.11 (m, 4H), 1.25 - 1.59 (m, 4H), 3.94 (s, 3H), 3.96 (s, 3H), 6.42 (d, J = 5.37 Hz, 1H), 7.42 (s, 1H), 7.47 (d, J = 8.78 Hz, 1H), 7.53 (s, 1H), 7.70 - 7.73 (m, 1H), 8.17 - 8.19 (m, 1H), 8.51 (d, J = 5.12 Hz, 1H), 11.58 (s, 1H), 12.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 503 (M⁺+1)

Example 1078: N-(2-Chlorobenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]thiourea

[1330] Commercially available 2-chloro-1-benzenecarbonyl isothiocyanate (50 μl) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (68 mg, yield 85%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.18 (s, 3H), 2.35 (s, 3H), 4.07 (s, 6H), 6.35 (d, J = 5.37 Hz, 1H), 7.07 (d, J = 8.54 Hz, 1H), 7.26 (s, 1H), 7.44 - 7.49 (m, 2H), 7.52 - 7.57 (m, 3H), 7.61 (s, 1H), 7.68 (d, J = 7.32 Hz, 1H), 8.48 (d, J = 5.37 Hz, 1H), 9.41 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 523 (M⁺+1)

Example 1079: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]-N'-(3-methylbenzoyl)thiourea

[1331] Commercially available 3-methyl-1-benzenecarbonyl isothiocyanate (50 μl) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (64 mg, yield 83%).

¹H-NMR (CDCl₃, 400 MHz) : δ 2.24 (s, 3H), 2.34 (s, 3H), 2.47 (s, 3H), 4.07 (s, 6H), 6.35 (d, J = 5.37 Hz, 1H), 7.06 (d, J = 8.54 Hz, 1H), 7.26 (s, 1H), 7.43 - 7.49 (m, 3H), 7.55 (d, J = 8.78 Hz, 1H), 7.61 (s, 1H), 7.71 - 7.74 (m, 2H), 8.48 (d, J = 5.12 Hz, 1H), 9.23 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

Example 1080: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}-N'-(4-methylbenzoyl)thiourea

[1332] Commercially available 4-methyl-1-benzenecarbonyl isothiocyanate (50 μ l) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (60 mg, yield 78%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.18 (s, 3H), 2.33 (s, 3H), 2.47 (s, 3H), 4.07 (s, 6H), 6.35 (d, J = 5.37 Hz, 1H), 7.26 (s, 2H), 7.37 (d, J = 7.81 Hz, 2H), 7.44 (s, 1H), 7.54 (d, J = 8.78 Hz, 1H), 7.61 (s, 1H), 7.83 (d, J = 8.29 Hz, 2H), 8.48 (d, J = 5.37 Hz, 1H), 9.22 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

Example 1081: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}-N'-(4-nitrobenzoyl)thiourea

[1333] Commercially available 4-nitro-1-benzenecarbonyl isothiocyanate (30 mg) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (62 mg, yield 75%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.42 (s, 3H), 2.34 (s, 3H), 4.07 (s, 6H), 6.35 (d, J = 5.12 Hz, 1H), 7.07 (d, J = 8.54 Hz, 1H), 7.27 (s, 2H), 7.44 (s, 1H), 7.52 (d, J = 8.54 Hz, 1H), 7.61 (s, 1H), 8.17 (d, J = 9.03 Hz, 2H), 8.42 (d, J = 9.03 Hz, 2H), 8.48 (d, J = 5.12 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 533 (M⁺+1)

Example 1082: N-(4-Chlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}thiourea

[1334] Commercially available 4-chloro-1-benzenecarbonyl isothiocyanate (50 μ l) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (55 mg, yield 68%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.19 (s, 3H), 2.33 (s, 3H), 4.06 (s, 6H), 6.35 (d, J = 5.12 Hz, 1H), 7.06 (d, J = 8.54 Hz, 1H), 7.26 (s, 1H), 7.44 (s, 1H), 7.51 - 7.56 (m, 3H), 7.61 (s, 1H), 7.89 (d, J = 11.22 Hz, 2H), 8.48 (d, J = 5.37 Hz, 1H), 9.22 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 523 (M⁺+1)

Example 1083: N-(3-Chlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}thiourea

[1335] Commercially available 3-chloro-1-benzenecarbonyl isothiocyanate (50 μ l) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (70 mg, yield 87%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.19 (s, 3H), 2.33 (s, 3H), 4.07 (s, 6H), 6.35 (d, J = 5.37 Hz, 1H), 7.06 (d, J = 8.54 Hz, 1H), 7.26 (s, 1H), 7.44 (s, 1H), 7.49 - 7.54 (m, 2H), 7.61 (s, 1H), 7.65 (d, J = 9.03 Hz, 1H), 7.80 (d, J = 10.49 Hz, 1H), 7.95 (s, 1H), 8.48 (d, J = 5.12 Hz, 1H), 9.24 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 523 (M⁺+1)

Example 1084: N-Benzoyl-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}thiourea

[1336] Commercially available 1-benzenecarbonyl isothiocyanate (50 μ l) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (50 mg, yield 67%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.19 (s, 3H), 2.34 (s, 3H), 4.07 (s, 6H), 6.35 (d, J = 5.37 Hz, 1H), 7.06 (d, J = 8.54 Hz, 1H), 7.26 (s, 1H), 7.44 (s, 1H), 7.49 - 7.61 (m, 4H), 7.67 - 7.70 (m, 1H), 7.94 (d, J = 8.54 Hz, 2H), 8.48 (d, J = 5.37 Hz, 1H), 9.27 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 488 (M⁺+1)

Example 1085: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]-N'-(2-methylbenzoyl)thiourea

[1337] Commercially available 2-methyl-1-benzenecarbonyl isothiocyanate (50 µl) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (61 mg, yield 79%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.19 (s, 3H), 2.35 (s, 3H), 2.59 (s, 3H), 4.07 (s, 6H), 6.35 (d, J = 5.37 Hz, 1H), 7.07 (d, J = 8.78 Hz, 1H), 7.26 (s, 1H), 7.33 - 7.36 (m, 2H), 7.45 - 7.49 (m, 2H), 7.55 - 7.61 (m, 3H), 8.48 (d, J = 5.12 Hz, 1H), 8.96 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

Example 1086: N-(2,4-Dichlorobenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]thiourea

[1338] 2,4-Dichloro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-dichloro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2,4-Dichloro-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (60 mg, yield 69%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.19 (s, 3H), 2.37 (s, 3H), 3.35 (s, 6H), 6.70 (d, J = 6.59 Hz, 1H), 7.11 (d, J = 8.54 Hz, 1H), 7.34 (dd, J = 1.95, 8.29 Hz, 1H), 7.45 - 7.48 (m, 2H), 7.56 - 7.72 (m, 5H), 8.54 (d, J = 6.31 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 557 (M⁺+1)

Example 1087: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]-N'-(4-methoxybenzoyl)thiourea

[1339] 4-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-Methoxy-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (55 mg, yield 69%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.09 (s, 3H), 2.22 (s, 3H), 3.86 (s, 3H), 3.95 (s, 6H), 6.29 (d, J = 5.37 Hz, 1H), 7.06 - 7.12 (m, 3H), 7.40 - 7.46 (m, 2H), 7.57 (s, 1H), 8.05 (d, J = 9.03 Hz, 2H), 8.47 (d, J = 5.37 Hz, 1H), 11.47 (bs, 1H), 3.95 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 518 (M⁺+1)

Example 1088: N-(2,4-Difluorobenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]thiourea

[1340] 2,4-Difluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-difluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2,4-Difluoro-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (60 mg, yield 74%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.17 (s, 3H), 2.34 (s, 3H), 4.09 (s, 3H), 4.11 (s, 3H), 6.49 (d, J = 6.59 Hz, 1H), 6.87 - 6.93 (m, 2H), 6.99 - 7.15 (m, 2H), 7.26 - 7.30 (m, 1H), 7.57 - 7.64 (m, 2H), 8.09 - 8.17 (m, 2H), 8.49 (d, J = 6.58 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 524 (M⁺+1)

Example 1089: N-(4-Chlorobenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-methylphenyl]thiourea

[1341] Commercially available 4-chloro-1-benzenecarbonyl isothiocyanate (50 µl) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (46 mg, yield 56%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.29 (s, 3H), 4.04 (s, 3H), 4.06 (s, 3H), 6.59 (d, J = 5.37 Hz, 1H), 7.09 - 7.12 (m, 2H), 7.26 (s, 1H), 7.44 (s, 1H), 7.53 - 7.58 (m, 3H), 7.83 - 7.89 (m, 3H), 8.53 (d, J = 5.37 Hz, 1H), 9.19 (bs, 1H)
Mass spectrometry value (ESI-MS, m/z): 509 (M⁺+1)

5 Example 1090: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylphenyl]-N'-(2-methylbenzoyl)thiourea

[1342] Commercially available 2-methyl-1-benzenecarbonyl isothiocyanate (50 μl) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (46 mg, yield 59%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.41 (s, 3H), 2.58 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), 6.59 (d, J = 5.37 Hz, 1H), 7.09 - 7.12 (m, 3H), 7.26 (s, 1H), 7.34 - 7.35 (m, 1H), 7.44 (s, 1H), 7.48 (t, J = 7.56 Hz, 1H), 7.53 (s, 1H), 7.59 (d, J = 7.81 Hz, 1H), 7.84 (d, J = 8.54 Hz, 1H), 8.53 (d, J = 5.12 Hz, 1H), 8.95 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 488 (M⁺+1)

Example 1091: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylphenyl]-N'-(3-fluorobenzoyl)thiourea

[1343] 3-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Fluoro-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (64 mg, yield 81%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.39 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), 6.59 (d, J = 5.37 Hz, 1H), 7.09 - 7.12 (m, 2H), 7.26 (s, 1H), 7.36 - 7.41 (m, 1H), 7.44 (s, 1H), 7.53 - 7.59 (m, 2H), 7.66 - 7.71 (m, 2H), 7.84 (d, J = 8.29 Hz, 1H), 8.54 (d, J = 5.12 Hz, 1H), 9.19 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 492 (M⁺+1)

Example 1092: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylphenyl]-N'-(4-nitrobenzoyl)thiourea

[1344] Commercially available 4-nitro-1-benzenecarbonyl isothiocyanate (30 mg) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (41 mg, yield 49%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.39 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), 6.59 (d, J = 5.37 Hz, 1H), 7.11 - 7.13 (m, 2H), 7.26 (s, 2H), 7.44 (s, 1H), 7.52 (s, 1H), 7.83 (d, J = 8.54 Hz, 1H), 8.13 (d, J = 9.03 Hz, 2H), 8.42 (d, J = 8.78 Hz, 2H), 8.54 (d, J = 5.37 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 519 (M⁺+1)

Example 1093: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylphenyl]-N'-(4-fluorobenzoyl)thiourea

[1345] 4-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-Fluoro-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (35 mg, yield 44%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.39 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), 6.59 (d, J = 5.37 Hz, 1H), 7.09 - 7.12 (m, 2H), 7.23 - 7.28 (m, 3H), 7.44 (s, 1H), 7.53 (s, 1H), 7.84 (d, J = 8.29 Hz, 1H), 7.96 - 7.99 (m, 2H), 8.53 (d, J = 5.37 Hz, 1H), 9.19 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

Example 1094: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylphenyl]-N'-(2-fluorobenzoyl)thiourea

[1346] 2-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature.

carbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (41 mg, yield 52%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.39 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), 6.59 (d, J = 5.37 Hz, 1H), 7.09 - 7.12 (m, 2H), 7.24 - 7.29 (m, 3H), 7.39 (t, J = 7.68 Hz, 1H), 7.44 (s, 1H), 7.53 (s, 1H), 7.64 - 7.69 (m, 1H), 7.86 (d, J = 8.29 Hz, 1H), 8.12 - 8.16 (m, 1H), 8.53 (d, J = 5.12 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 492 (M⁺+1)

Example 1095: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylphenyl]-N'-(4-methoxybenzoyl)thiourea

[1347] 4-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-Methoxy-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (37 mg, yield 45%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.40 (s, 3H), 3.92 (s, 6H), 4.05 (s, 3H), 7.03 - 7.11 (m, 4H), 7.26 (s, 5H), 7.56 (s, 1H), 7.90 - 7.92 (m, 3H)

Mass spectrometry value (ESI-MS, m/z): 504 (M⁺+1)

Example 1096: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylphenyl]-N'-(4-methylbenzoyl)thiourea

[1348] Commercially available 4-methyl-1-benzenecarbonyl isothiocyanate (50 μl) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (44 mg, yield 56%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.39 (s, 3H), 2.47 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), 6.59 (d, J = 5.37 Hz, 1H), 7.08 - 7.12 (m, 2H), 7.26 (s, 1H), 7.36 (d, J = 7.81 Hz, 2H), 7.44 (s, 1H), 7.53 (s, 1H), 7.81 - 7.86 (m, 3H), 8.53 (d, J = 5.12 Hz, 1H), 9.19 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 488 (M⁺+1)

Example 1097: N-(2-Chlorobenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-methylphenyl]thiourea

[1349] Commercially available 2-chloro-1-benzenecarbonyl isothiocyanate (50 μl) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (47 mg, yield 57%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.41 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), 6.59 (d, J = 5.12 Hz, 1H)¹, 7.09 - 7.12 (m, 2H), 7.26 (s, 2H), 7.44 - 7.48 (m, 2H), 7.53 - 7.54 (m, 2H), 7.82 (d, J = 7.08 Hz, 1H), 7.88 (d, J = 8.54 Hz, 1H), 8.54 (d, J = 5.12 Hz, 1H), 9.38 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 508 (M⁺+1)

Example 1098: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylphenyl]-N'-(3-methylbenzoyl)thiourea

[1350] Commercially available 3-methyl-1-benzenecarbonyl isothiocyanate (50 μl) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (32 mg, yield 40%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.39 (s, 3H), 2.47 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), 6.59 (d, J = 5.37 Hz, 1H), 7.09 - 7.12 (m, 2H), 7.26 (s, 1H), 7.44 - 7.49 (m, 3H), 7.53 (s, 1H), 7.71 - 7.74 (m, 2H), 7.87 (d, J = 8.29 Hz, 1H), 8.53 (d, J = 5.37 Hz, 1H), 9.21 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 488 (M⁺+1)

Example 1099: N-Benzoyl-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-methylphenyl}thiourea

[1351] Commercially available 1-benzenecarbonyl isothiocyanate (50 µl) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (44 mg, yield 58%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.39 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), 6.59 (d, J = 5.37 Hz, 1H), 7.09 - 7.12 (m, 3H), 7.25 (s, 1H), 7.44 (s, 1H), 7.53 (s, 1H), 7.58 (t, J = 7.08 Hz, 2H), 7.68 (t, J = 7.32 Hz, 1H), 7.86 (d, J = 8.29 Hz, 2H), 7.94 (d, J = 8.54 Hz, 1H), 9.23 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 474 (M⁺+1)

Example 1100: N-(3-Chlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-methylphenyl}thiourea

[1352] Commercially available 3-chloro-1-benzenecarbonyl isothiocyanate (50 µl) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (41 mg, yield 50%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.39 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), 6.59 (d, J = 5.12 Hz, 1H), 7.09 - 7.12 (m, 2H), 7.27 (s, 1H), 7.44 (s, 1H), 7.49 - 7.54 (m, 2H), 7.65 (d, J = 8.05 Hz, 1H), 7.79 (d, J = 8.29 Hz, 1H), 7.85 (d, J = 8.54 Hz, 1H), 7.95 (s, 1H), 8.53 (d, J = 5.37 Hz, 1H), 9.19 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 508 (M⁺+1)

Example 1101: N-{2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-methylbenzoyl)thiourea

[1353] Commercially available 2-methyl-1-benzenecarbonyl isothiocyanate (50 µl) was dissolved in ethanol (1 ml) to prepare a solution. 2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (40 mg, yield 52%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.64 (s, 3H), 3.92 (s, 3H), 3.93 (s, 3H), 6.60 (d, J = 5.12 Hz, 1H), 7.19 - 7.21 (m, 2H), 7.34 (m, 2H), 7.41 - 7.47 (m, 3H), 7.52 (m, 2H), 8.16 - 8.20 (m, 1H), 8.52 - 8.53 (m, 2H)

Mass spectrometry value (ESI-MS, m/z): 508 (M⁺+1)

Example 1102: N-{2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(4-methylbenzoyl)thiourea

[1354] Commercially available 4-methyl-1-benzenecarbonyl isothiocyanate (50 µl) was dissolved in ethanol (1 ml) to prepare a solution. 2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (38 mg, yield 49%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.41 (s, 3H), 3.94 (s, 3H), 3.97 (s, 3H), 6.69 (d, J = 5.37 Hz, 1H), 7.33 - 7.37 (m, 4H), 7.44 (s, 1H), 7.54 (s, 1H), 7.60 (d, J = 2.68 Hz, 1H), 7.94 (d, J = 8.29 Hz, 1H), 8.14 (d, J = 9.03 Hz, 1H), 8.59 (d, J = 5.37 Hz, 1H), 11.74 (s, 1H), 12.75 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 509 (M⁺+1)

Example 1103: N-{2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-methoxybenzoyl)thiourea

[1355] 2-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Methoxy-1-benzenecarbonyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (36 mg, yield 45%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 4.04 (s, 3H), 6.42 (d, J = 5.12 Hz, 1H), 7.18 (t, J = 7.69 Hz, 1H), 7.30 (d, J = 8.54 Hz, 1H), 7.41 (s, 1H), 7.48 (d, J = 8.76 Hz, 1H), 7.52 (s, 1H), 7.68 (t, J = 6.96 Hz, 1H), 7.76 (dd, J = 2.56, 8.90 Hz, 1H), 7.94 (d, J = 7.81 Hz, 1H), 8.20 (d, J = 2.44 Hz, 1H), 8.49 (d, J = 5.12 Hz, 1H), 11.29

(s, 1H), 12.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 525 (M⁺+1)

Example 1104: N-(2-Chlorobenzoyl)-N'-[2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]thiourea

[1356] Commercially available 2-chloro-1-benzenecarbonyl isothiocyanate (50 µl) was dissolved in ethanol (1 ml) to prepare a solution. 2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (38 mg, yield 48%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.93 (s, 3H), 4.05 (s, 3H), 6.67 (d, J = 5.12 Hz, 1H), 7.20 (d, J = 7.81 Hz, 1H), 7.32 - 7.36 (m, 2H), 7.43 (s, 1H), 7.47 (s, 1H), 7.54 - 7.66 (m, 2H), 7.67 (d, J = 6.59 Hz, 1H), 8.13 (d, J = 8.78 Hz, 1H), 8.58 (d, J = 5.12 Hz, 1H), 12.23 (s, 1H), 12.36 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 529 (M⁺+1)

Example 1105: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl}-N'-(2-phenylacetyl)thiourea

[1357] 2-Phenylethanoyl isothiocyanate was prepared using commercially available 2-phenylethanoyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-phenylethanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (44 mg, yield 58%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.08 (s, 3H), 2.15 (s, 3H), 3.85 (s, 2H), 3.94 (s, 3H), 3.95 (s, 3H), 6.28 (d, J = 5.12 Hz, 1H), 7.08 (d, J = 8.54 Hz, 1H), 7.27 - 7.41 (m, 7H), 7.57 (s, 1H), 8.47 (d, J = 5.37 Hz, 1H), 11.75 (bs, 1H), 12.01 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

Example 1106: N-{2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(3-cyclopentylpropanoyl)thiourea

[1358] 3-Cyclopentylpropanoyl isothiocyanate was prepared using commercially available 3-cyclopentylpropanoyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Cyclopentylpropanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (32 mg, yield 41%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.11 (m, 2H), 1.49 - 1.61 (m, 7H), 1.63 - 1.79 (m, 4H), 3.92 (s, 3H), 3.93 (s, 3H), 6.65 (d, J = 5.37 Hz, 1H), 7.31 (d, J = 11.71 Hz, 1H), 7.47 (s, 1H), 7.48 (s, 1H), 7.58 (d, J = 2.68 Hz, 1H), 8.12 (d, J = 8.78 Hz, 1H), 8.56 (d, J = 6.83 Hz, 1H), 11.67 (s, 1H), 12.53 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 515 (M⁺+1)

Example 1107: N-Benzoyl-N'-[2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]thiourea

[1359] Commercially available 1-benzenecarbonyl isothiocyanate (50 µl) was dissolved in ethanol (1 ml) to prepare a solution. 2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (36 mg, yield 48%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.92 (s, 3H), 3.96 (s, 3H), 6.66 (d, J = 5.37 Hz, 1H), 7.32 (d, J = 8.78 Hz, 1H), 7.42 (s, 1H), 7.48 (s, 1H), 7.53 - 7.57 (m, 3H), 7.66 - 7.68 (m, 1H), 8.02 (d, J = 8.54 Hz, 2H), 8.13 (d, J = 9.03 Hz, 1H), 8.56 (d, J = 5.37 Hz, 1H), 11.38 (s, 1H), 12.70 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 495 (M⁺+1)

Example 1108: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylphenyl}-N'-(4-nitrobenzoyl)thiourea

[1360] Commercially available 4-nitro-1-benzenecarbonyl isothiocyanate (30 mg) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated,

and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (79 mg, yield 94%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.17 (s, 3H), 3.96 (s, 6H), 6.36 (d, J = 5.12 Hz, 1H), 7.41 (s, 1H), 7.57 (s, 2H), 7.72 (bs, 2H), 8.19 (d, J = 8.78 Hz, 2H), 8.29 (s, 1H), 8.36 (d, J = 8.54 Hz, 2H), 8.48 (d, J = 5.12 Hz, 2H)

Mass spectrometry value (ESI-MS, m/z): 519 (M⁺+1)

Example 1109: N-Benzoyl-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-methylphenyl}thiourea

[1361] Commercially available 1-benzenecarbonyl isothiocyanate (50 μl) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (61 mg, yield 80%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.24 (s, 3H), 4.09 (s, 3H), 4.12 (s, 3H), 6.58 (d, J = 6.09 Hz, 1H), 7.26 (s, 1H), 7.56 - 7.81 (m, 8H), 7.93 (d, J = 7.32 Hz, 2H), 8.49 (d, J = 5.86 Hz, 1H), 9.14 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 474 (M⁺+1)

Example 1110: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylphenyl}-N'-(3-methylbenzoyl)thiourea

[1362] Commercially available 3-methyl-1-benzenecarbonyl isothiocyanate (50 μl) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (65 mg, yield 83%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.17 (s, 3H), 2.41 (s, 3H), 3.96 (s, 6H), 6.37 (d, J = 4.88 Hz, 1H), 7.33 (d, J = 9.02 Hz, 1H), 7.41 - 7.48 (m, 4H), 7.56 (s, 1H), 7.72 - 7.85 (m, 3H), 8.48 (d, J = 5.37 Hz, 1H), 11.53 (s, 1H), 12.67 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 488 (M⁺+1)

Example 1111: N-(4-Chlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-methylphenyl}thiourea

[1363] Commercially available 4-chloro-1-benzenecarbonyl isothiocyanate (50 μl) was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-methylaniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (52 mg, yield 64%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.24 (s, 3H), 4.08 (s, 3H), 4.09 (s, 3H), 6.44 (d, J = 5.37 Hz, 1H), 7.17 (d, J = 8.54 Hz, 1H), 7.26 (s, 1H), 7.55 (d, J = 8.29 Hz, 3H), 7.62 (d, J = 7.81 Hz, 3H), 7.71 (d, J = 7.81 Hz, 1H), 7.87 (d, J = 8.54 Hz, 1H), 8.49 (d, J = 5.61 Hz, 1H), 9.11 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 508 (M⁺+1)

Example 1112: N-(2,6-Dichlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}thiourea

[1364] 2,6-Dichloro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,6-dichloro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2,6-dichloro-1-benzenecarbonyl in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (55 mg, yield 63%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 6.52 (d, J = 5.12 Hz, 1H), 7.38 - 7.79 (m, 7H), 8.07 - 8.10 (m, 1H), 8.52 (d, J = 5.12 Hz, 1H), 12.30 (bs, 1H), 12.43 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 547 (M⁺+1)

Example 1113: N-(2,4-Dimethoxybenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}thiourea

[1365] 2,4-Dimethoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-dimethoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare

a solution. A solution of 2,4-dimethoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (45 mg, yield 53%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.87 (s, 3H), 3.90 (s, 3H), 3.96 (s, 3H), 4.06 (s, 3H), 6.52 (d, J = 6.34 Hz, 1H), 6.79 - 6.81 (m, 2H), 7.43 (s, 2H), 7.50 - 7.55 (m, 1H), 7.64 (d, J = 11.22 Hz, 1H), 7.99 (d, J = 9.03 Hz, 1H), 8.11 (d, J = 14.64 Hz, 1H), 8.52 (d, J = 5.12 Hz, 1H), 11.09 (bs, 1H), 12.76 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 538 (M⁺+1)

Example 1114: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2,4-dichlorobenzoyl)thiourea

[1366] 2,4-Dichloro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-dichloro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2,4-dichloro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (53 mg, yield 62%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 6.43 (d, J = 5.12 Hz, 1H), 7.43 - 8.17 (m, 7H), 8.17 (bs, 1H), 8.52 (d, J = 5.12 Hz, 1H), 12.13 (bs, 1H), 12.28 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 563 (M⁺+1)

Example 1115: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2,6-dichlorobenzoyl)thiourea

[1367] 2,6-Dichloro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,6-dichloro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2,6-dichloro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (40 mg, yield 47%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 6.43 (d, J = 5.37 Hz, 1H), 7.43 (s, 1H), 7.47 - 7.61 (m, 5H), 7.77 - 7.98 (m, 1H), 8.18 - 8.20 (m, 1H), 8.52 (d, J = 5.12 Hz, 1H), 12.24 (bs, 1H), 12.43 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 563 (M⁺+1)

Example 1116: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(3,5-dichlorobenzoyl)thiourea

[1368] 3,5-Dichloro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3,5-dichloro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3,5-dichloro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (55 mg, yield 63%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 6.42 (d, J = 4.64 Hz, 1H), 7.42 (s, 1H), 7.49 (d, J = 8.78 Hz, 1H), 7.53 (s, 1H), 7.72 - 8.00 (m, 6H), 8.16 (bs, 1H), 8.50 (d, J = 5.12 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 563 (M⁺+1)

Example 1117: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2,4-dimethoxybenzoyl)thiourea

[1369] 2,4-Dimethoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-dimethoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2,4-dimethoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (53 mg, yield 63%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.90 (s, 3H), 3.95 (s, 3H), 3.96 (s, 3H), 4.06 (s, 3H), 6.43 (d, J = 5.12 Hz, 1H),

6.73 - 6.81 (m, 2H), 7.43 (s, 1H), 7.49 - 7.53 (m, 3H), 7.78 (dd, J = 2.44 Hz, J = 8.78 Hz, 1H), 8.12 (bs, 1H), 8.51 (d, J = 5.12 Hz, 1H), 11.09 (bs, 1H), 12.69 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 555 (M⁺+1)

5 Example 1118: N-(2,6-Dichlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1370] 2,6-Dichloro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,6-dichloro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2,6-dichloro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (57 mg, yield 64%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 4.09 (s, 3H), 4.13 (s, 3H), 6.69 (d, J = 6.09 Hz, 1H), 7.11 - 7.44 (m, 6H), 7.62 (s, 1H), 7.79 - 7.98 (m, 3H), 8.52 (d, J = 6.34 Hz, 1H), 8.81 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 529 (M⁺+1)

Example 1119: N-(2,4-Dimethoxybenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1371] 2,4-Dimethoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-dimethoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2,4-dimethoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (42 mg, yield 48%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.90 (s, 3H), 3.93 (s, 3H), 3.95 (s, 3H), 4.06 (s, 3H), 6.56 (d, J = 5.37 Hz, 1H), 6.79 - 6.81 (m, 2H), 7.33 (d, J = 9.03 Hz, 2H), 7.41 (s, 1H), 7.50 (s, 1H), 7.84 (d, J = 8.78 Hz, 2H), 8.01 (d, J = 9.03 Hz, 1H), 8.52 (d, J = 5.12 Hz, 1H), 11.05 (bs, 1H), 12.67 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 520 (M⁺+1)

Example 1120: N-(3,4-Dichlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1372] 3,4-Dichloro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3,4-dichloro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3,4-dichloro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (56 mg, yield 63%).

¹H-NMR (CDCl₃, 400 MHz): δ 4.05 (s, 3H), 4.06 (s, 3H), 6.62 (d, J = 5.37 Hz, 1H), 7.24 (s, 1H), 7.26 (s, 1H), 7.61 - 7.68 (m, 6H), 7.73 (m, 1H), 7.81 (d, J = 9.03 Hz, 1H), 8.04 (d, J = 1.95 Hz, 1H), 8.54 (d, J = 5.12 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 529 (M⁺+1)

Example 1121: N-(2,4-Difluorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}thiourea

[1373] 2,4-Difluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-difluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2,4-difluoro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (56 mg, yield 68%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.93 (s, 3H), 3.96 (s, 3H), 6.66 (d, J = 5.12 Hz, 1H), 7.13 - 7.84 (m, 7H), 8.04 (m, 1H), 8.56 (d, J = 5.12 Hz, 1H), 11.95 (s, 1H), 12.18 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 514 (M⁺+1)

Example 1122: N-(3,5-Dichlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}thiourea

[1374] 3,5-Dichloro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3,5-dichloro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3,5-dichloro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (51 mg, yield 64%).

Mass spectrometry value (ESI-MS, m/z): 547 (M⁺+1)

Example 1123: N-(2,4-Dimethoxybenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}thiourea

[1375] 2,4-Dimethoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-dimethoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2,4-dimethoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (54 mg, yield 67%).

Mass spectrometry value (ESI-MS, m/z) : 538 (M⁺+1)

Example 1124: N-(4-Cyclohexylbenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1376] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-cyclohexylbenzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-cyclohexyl-1-benzenecarbonyl isothiocyanate was prepared using the resultant 4-cyclohexyl-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-cyclohexyl-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (44 mg, yield 48%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.31 - 1.83 (m, 11H), 3.93 (s, 3H), 3.95 (s, 3H), 6.56 (d, J = 5.12 Hz, 1H), 7.31 (d, J = 8.54 Hz, 3H), 7.39 (d, J = 6.83 Hz, 4H), 7.49 (s, 1H), 7.83 (m, 3H), 7.95 (d, J = 8.05 Hz, 3H), 8.50 (d, J = 5.12 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z) : 542 (M⁺+1)

Example 1125: N-(4-Phenylbenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]-2-fluorophenyl}thiourea

[1377] 4-Phenyl-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-phenyl-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-phenyl-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (41 mg, yield 47%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.93 (s, 3H), 3.96 (s, 3H), 6.67 (d, J = 5.12 Hz, 1H), 7.19 (m, 1H), 7.43 - 7.53 (m, 7H), 7.78 (d, J = 7.81 Hz, 2H), 7.86 (d, J = 8.19 Hz, 2H), 8.11 - 8.13 (m, 2H), 8.56 (d, J = 5.37 Hz, 1H), 11.87 (s, 1H), 12.57 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 554 (M⁺+1)

Example 1126: N-(1,3-Benzodioxol-5-ylcarbonyl)-N'-{3-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1378] 1,3-Benzodioxole-5-carbonyl isothiocyanate was prepared using commercially available 1,3-benzodioxole-5-carbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 1,3-benzodioxole-5-carbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (47 mg, yield

58%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 6.18 (s, 2H), 6.42 (d, J = 5.12 Hz, 1H), 7.08 (d, J = 8.48 Hz, 1H), 7.43 (s, 1H), 7.50 (d, J = 8.78 Hz, 1H), 7.54 (s, 1H), 7.57 (s, 1H), 7.67 (d, J = 8.29 Hz, 1H), 7.74 (d, J = 9.03 Hz, 1H), 8.19 (bs, 1H), 8.51 (d, J = 5.12 Hz, 1H), 11.49 (bs, 1H), 12.67 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 538 (M⁺+1)

Example 1127: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(4-cyclohexylbenzoyl)thiourea

[1379] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-cyclohexylbenzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-cyclohexyl-1-benzenecarbonyl isothiocyanate was prepared using the resultant 4-cyclohexyl-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-cyclohexyl-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (47 mg, yield 54%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.31 - 1.83 (m, 11H), 3.95 (s, 6H), 6.41 (d, J = 4.88 Hz, 1H), 7.39 (d, J = 9.27 Hz, 4H), 7.47 (d, J = 8.54 Hz, 1H), 7.73 (m, 1H), 7.95 (d, J = 7.56 Hz, 2H), 8.21 (m, 1H), 8.49 (d, J = 5.61 Hz, 1H), 11.54 (s, 1H), 12.74 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 577 (M⁺+1)

Example 1128: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(4-octylbenzoyl)thiourea

[1380] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-octylbenzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-octyl-1-benzenecarbonyl isothiocyanate was prepared using the resultant 4-octyl-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-octyl-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (47 mg, yield 54%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.83 - 0.88 (m, 4H), 1.25 - 1.28 (m, 7H), 1.58 - 1.60 (m, 3H), 2.60 - 2.69 (m, 3H), 3.91 (s, 3H), 3.96 (s, 3H), 6.57 (d, J = 5.12 Hz, 1H), 7.25 (d, J = 8.05 Hz, 1H), 7.32 - 7.42 (m, 4H), 7.51 (s, 1H), 7.58 (s, 1H), 7.78 (d, J = 8.05 Hz, 1H), 7.84 - 7.86 (m, 2H), 7.94 (d, J = 8.05 Hz, 2H), 8.53 (d, J = 5.37 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 572 (M⁺+1)

Example 1129: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(3,5-dimethylbenzoyl)thiourea

[1381] Toluene (20 ml) and thionyl chloride (1 ml) was added to commercially available 3,5-dimethylbenzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3,5-dimethyl-1-benzenecarbonyl isothiocyanate was prepared using the resultant 3,5-dimethyl-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3,5-dimethyl-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (39 mg, yield 47%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.37 (s, 6H), 3.95 (s, 3H), 3.96 (s, 3H), 6.41 {d, J = 5.37 Hz, 1H}, 7.29 (s, 1H), 7.41 (s, 1H), 7.47 (d, J = 8.78 Hz, 1H), 7.53 (s, 1H), 7.63 (s, 2H), 7.71 - 7.74 (m, 2H), 8.19 - 8.20 (m, 1H), 8.50 (d, J = 5.37 Hz, 1H), 11.54 (s, 1H), 12.72 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 488 (M⁺+1)

Example 1130: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(1,2,3,4-tetrahydro-2-isoquinolylcarbonyl)thiourea

[1382] Commercially available 1,2,3,4-tetrahydroisoquinoline (50 mg) was dissolved in chloroform (10 ml), and triphosgene (111 mg) was added to the solution. The mixture was stirred at room temperature for 2 hr. The solvent was removed by distillation to give 1,2,3,4-tetrahydro-2-isoquinolinecarbonyl chloride. 1,2,3,4-Tetrahydro-2-isoquinolinecarbonyl isothiocyanate was prepared using this compound as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare

a solution. A solution of 1,2,3,4-tetrahydro-2-isoquinolinecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (78 mg, yield 94%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.81 - 2.89 (m, 4H), 3.92 (s, 3H), 3.94 (s, 3H), 4.87 (m, 2H), 6.52 (d, J = 5.12 Hz, 1H), 7.13 - 7.28 (m, 4H), 7.39 - 7.49 (m, 4H), 7.73 (d, J = 8.29 Hz, 2H), 8.49 (d, J = 5.12 Hz, 1H), 10.18 (bs, 1H), 12.51 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 515 (M⁺+1)

Example 1131: N-(3-Cyclopentylpropanoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1383] 3-Cyclopentylpropanoyl isothiocyanate was prepared using commercially available 3-cyclopentylpropanoyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-cyclopentylpropanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (46 mg, yield 57%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.11 (m, 1H), 1.50 - 1.76 (m, 8H), 2.32 - 2.33 (m, 2H), 2.67 - 2.68 (m, 2H), 3.95 (s, 3H), 3.98 (s, 3H), 6.51 (d, J = 4.39 Hz, 1H), 6.79 (d, J = 2.68 Hz, 1H), 7.39 - 7.52 (m, 4H), 8.04 (d, J = 12.20 Hz, 1H), 8.52 (d, J = 5.37 Hz, 1H), 11.58 (bs, 1H), 12.65 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 480 (M⁺+1)

Example 1132: N-(3-Cyclopentylpropanoyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}thiourea

[1384] 3-Cyclopentylpropanoyl isothiocyanate was prepared using commercially available 3-cyclopentylpropanoyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-cyclopentylpropanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (37 mg, yield 46%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.28 - 1.32 (m, 1H), 1.48 - 1.63 (m, 5H), 1.73 - 1.79 (m, 3H), 2.32 - 2.33 (m, 2H), 2.67 - 2.68 (m, 2H), 3.98 (s, 3H), 3.99 (s, 3H), 7.34 - 7.39 (m, 3H), 7.58 (s, 2H), 7.71 - 7.75 (m, 2H), 8.57 (s, 2H), 11.48 (bs, 1H), 12.54 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 481 (M⁺+1)

Example 1133: N-{4-[(6,7-Dimethoxy-4-quinazolinyloxy]phenyl}-N'-[3-(2-methylphenyl)propanoyl]thiourea

[1385] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-(2-methylphenyl)propanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-(2-methylphenyl)propanoyl isothiocyanate was prepared using the resultant 3-(2-methylphenyl)propanoyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-(2-methylphenyl)propanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (48 mg, yield 57%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.32 (s, 3H), 2.59 - 2.63 (m, 2H), 2.89 - 2.94 (m, 2H), 3.93 (s, 3H), 3.99 (s, 3H), 7.09 - 7.24 (m, 7H), 7.38 (s, 1H), 7.55 (s, 1H), 7.67 (d, J = 8.78 Hz, 2H), 8.53 (s, 1H), 10.03 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 503 (M⁺+1)

Example 1134: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}-N'-[3-(2-methylphenyl)propanoyl]thiourea

[1386] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-(2-methylphenyl)propanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-(2-methylphenyl)propanoyl isothiocyanate was prepared using the resultant 3-(2-methylphenyl)propanoyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-(2-methylphenyl)propanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica

gel using chloroform/acetone for development to give the title compound (45 mg, yield 54%)

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.33 (s, 3H), 2.75 - 2.79 (m, 2H), 2.87 - 2.91 (m, 2H), 3.95 (s, 3H), 3.96 (s, 3H), 6.51 (d, J = 5.12 Hz, 1H), 7.11 - 7.16 (m, 5H), 7.42 (s, 1H), 7.48 - 7.57 (m, 2H), 8.04 (d, J = 14.63 Hz, 1H), 8.51 (d, J = 5.37 Hz, 1H), 11.64 (s, 1H), 12.62 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 520 (M⁺+1)

Example 1135: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-[3-(methylsulphenyl)propanoyl]thiourea

[1387] 3-(Methylsulphenyl)propanoyl isothiocyanate was prepared using commercially available 3-(methylsulphenyl)propanoyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-(methylsulphenyl)propanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (41 mg, yield 56%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.05 (s, 3H), 2.73 - 2.82 (m, 4H), 4.02 (s, 3H), 4.04 (s, 3H), 6.84 (m, 1H), 7.35 (d, J = 7.32 Hz, 1H), 7.45 (d, J = 7.32 Hz, 1H), 7.53 (s, 1H), 7.73 (s, 1H), 7.86 - 7.90 (m, 4H), 8.79 (d, J = 5.13 Hz, 1H)

Mass spectrometry value (ESI-MS, m/z): 458 (M⁺+1)

Example 1136: N-[4-(Chloromethyl)benzoyl]-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]thiourea

[1388] 4-(Chloromethyl)-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-(chloromethyl)-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-(chloromethyl)-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (54 mg, yield 63%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.98 (s, 3H), 4.00 (s, 3H), 4.44 (s, 2H), 6.72 (d, J = 5.86 Hz, 1H), 7.40 (d, J = 8.54 Hz, 2H), 7.47 (s, 1H), 7.58 - 7.63 (m, 3H), 7.88 - 7.89 (m, 2H), 8.03 (d, J = 8.29 Hz, 2H), 8.67 (d, J = 5.61 Hz, 1H), 11.68 (bs, 1H), 12.62 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 508 (M⁺+1)

Example 1137: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-4-(chloromethyl)benzoyl]thiourea

[1389] 4-(Chloromethyl)-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-(chloromethyl)-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-(chloromethyl)-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (52 mg, yield 63%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.99 (s, 3H), 4.00 (s, 3H), 4.45 (s, 2H), 6.62 (d, J = 5.85 Hz, 1H), 7.48 (s, 1H), 7.57 - 7.65 (m, 4H), 7.82 (m, 1H), 8.03 (d, J = 7.47 Hz, 2H), 8.25 (m, 1H), 8.66 (d, J = 5.86 Hz, 1H), 11.77 (bs, 1H), 12.62 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 543 (M⁺+1)

Example 1138: N-[4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl]-N'-[2-(2-methylphenoxy)acetyl]thiourea

[1390] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-methylphenoxy)acetic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-methylphenoxy)ethanoyl isothiocyanate was prepared using the resultant 2-(2-methylphenoxy)ethanoyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-(2-methylphenoxy)ethanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (37 mg, yield 44%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.22 (s, 3H), 3.96 (s, 3H), 3.98 (s, 3H), 4.44 (s, 2H), 6.62 (d, J = 8.78 Hz, 2H), 6.80 - 6.93 (m, 5H), 7.11 - 7.16 (m, 2H), 7.35 (s, 1H), 7.39 (bs, 1H), 7.52 (s, 1H), 8.51 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 505 (M⁺+1)

Example 1139: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(4-phenylbutanoyl)thiourea

[1391] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-phenylbutanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-phenylbutanoyl isothiocyanate was prepared using the resultant 4-phenylbutanoyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-phenylbutanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (37 mg, yield 45%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.85 - 1.93 (m, 3H), 2.59 - 2.68 (m, 3H), 3.98 (s, 3H), 3.99 (s, 3H), 6.76 (d, J = 8.78 Hz, 1H), 7.19 - 7.36 (m, 6H), 7.39 (s, 1H), 7.57 (s, 1H), 7.73 (d, J = 8.78 Hz, 2H), 8.57 (s, 1H), 11.49 (s, 1H), 12.51 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 503 (M⁺+1)

Example 1140: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N-ethyl-N'-(4-phenylbutanoyl)thiourea

[1392] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-phenylbutanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-phenylbutanoyl isothiocyanate was prepared using the resultant 4-phenylbutanoyl chloride as a starting compound according to the description of the literature. N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N-ethylamine (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-phenylbutanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (45 mg, yield 56%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.15 - 1.19 (m, 3H), 1.52 (m, 2H), 2.04 - 2.09 (m, 2H), 2.21 - 2.33 (m, 2H), 3.85 (s, 3H), 3.94 (s, 3H), 4.21 (bs, 1H), 6.40 (d, J = 5.12 Hz, 1H), 7.08 - 7.40 (m, 12H), 8.33 (d, J = 4.88 Hz, 1H), 10.48 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 530 (M⁺+1)

Example 1141: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[3-(2-methoxyphenyl)propanoyl]thiourea

[1393] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-(2-methoxyphenyl)propanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-(2-methoxyphenyl)propanoyl isothiocyanate was prepared using the resultant 4-phenylbutanoyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-(2-methoxyphenyl)propanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (37 mg, yield 43%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.73 - 2.77 (m, 2H), 2.85 - 2.89 (m, 2H), 3.92 (s, 3H), 3.98 (s, 3H), 3.99 (s, 3H), 6.87 - 6.91 (m, 2H), 6.97 (d, J = 8.29 Hz, 1H), 7.17 - 7.23 (m, 1H), 7.36 (d, J = 8.78 Hz, 2H), 7.39 (s, 1H), 7.57 (s, 1H), 7.73 (d, J = 8.78 Hz, 2H), 8.57 (s, 1H), 11.51 (bs, 1H), 12.52 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 519 (M⁺+1)

Example 1142: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N-ethyl-N'-[3-(2-methoxyphenyl)propanoyl]thiourea

[1394] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-(2-methoxyphenyl)propanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-(2-methoxyphenyl)propanoyl isothiocyanate was prepared using the resultant 4-phenylbutanoyl chloride as a starting compound according to the description of the literature. N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N-ethylamine (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-(2-methoxyphenyl)propanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (44 mg, yield 52%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.19 - 1.18 (m, 3H), 2.32 (m, 2H), 2.52 - 2.54 (m, 2H), 3.72 (s, 3H), 3.93 (s, 3H), 3.97 (s, 3H), 6.51 (d, J = 5.37 Hz, 1H), 6.82 - 6.85 (m, 1H), 6.91 (d, J = 7.56 Hz, 1H), 6.95 - 6.99 (m, 1H), 7.00 -

7.19 (m, 7H), 7.42 (s, 1H), 7.53 (s, 1H), 8.42 (bs, 1H), 10.49 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 546 (M⁺+1)

Example 1143: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N-ethyl-N'-[(2-phenylcyclopropyl)carbonyl]thiourea

[1395] 2-Phenyl-1-cyclopropanecarbonyl isothiocyanate was prepared using commercially available 2-phenyl-1-cyclopropanecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N-ethylamine (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-phenyl-1-cyclopropanecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (43 mg, yield 53%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.60 - 1.19 (m, 3H), 1.23 (m, 2H), 1.91 (m, 2H), 1.91 (bs, 2H), 3.91 (s, 3H), 3.95 (s, 3H), 4.21 (m, 2H), 6.46 (d, J = 5.12 Hz, 1H), 7.03 (d, J = 7.56 Hz, 2H), 7.15 - 7.33 (m, 5H), 7.42 (s, 1H), 7.50 (s, 1H), 8.45 (d, J = 5.37 Hz, 1H), 10.78 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 528 (M⁺+1)

Example 1144: N-[2-(2-Chlorophenoxy)propanoyl]-N'-[4-[(6,7-dimethoxy-4-quinazolyl)oxy]phenyl]thiourea

[1396] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-chlorophenoxy)propanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-chlorophenoxy)propanoyl isothiocyanate was prepared using the resultant 2-(2-chlorophenoxy)propanoyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-(2-chlorophenoxy)propanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (45 mg, yield 50%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.61 (d, J = 6.59 Hz, 3H), 3.93 (s, 3H), 3.98 (s, 3H), 5.21 - 5.22 (m, 1H), 6.99 - 7.05 (m, 2H), 7.32 - 7.35 (m, 3H), 7.38 (s, 1H), 7.47 (d, J = 8.05 Hz, 1H), 7.70 - 7.74 (m, 3H), 8.55 (s, 1H), 11.65 (bs, 1H), 12.09 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 540 (M⁺+1)

Example 1145: N-(1,3-Benzodioxol-5-ylcarbonyl)-N'-[4-[(6,7-dimethoxy-4-quinolyl)oxy]-3-fluorophenyl]thiourea

[1397] 1,3-Benzodioxole-5-carbonyl isothiocyanate was prepared using commercially available 1,3-benzodioxole-5-carbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 1,3-benzodioxole-5-carbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (62 mg, yield 75%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 6.18 (s, 2H), 6.52 (d, J = 4.88 Hz, 1H), 7.09 (d, J = 8.30 Hz, 1H), 7.43 (s, 1H), 7.49 - 7.61 (m, 4H), 7.67 (d, J = 1.87 Hz, J = 7.29 Hz, 1H), 8.08 (d, J = 11.22 Hz, 1H), 8.52 (d, J = 5.16 Hz, 1H), 11.49 (bs, 1H), 12.72 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 522 (M⁺+1)

Example 1146: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl]-N'-[(5-methyl-2-thienyl)carbonyl]thiourea

[1398] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 5-methyl-2-thiophenecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 5-methyl-2-thiophenecarbonyl isothiocyanate was prepared using the resultant 5-methyl-2-thiophenecarbonyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 5-methyl-2-thiophenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (42 mg, yield 52%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.51 (s, 3H), 4.01 (s, 6H), 6.78 - 6.82 (m, 1H), 6.96 (s, 1H), 6.99 (s, 1H), 7.53 - 7.65 (m, 3H), 7.91 (d, J = 3.42 Hz, 1H), 8.14 (d, J = 10.98 Hz, 1H), 8.24 (d, J = 3.42 Hz, 1H), 8.71 (d, J = 5.86 Hz, 1H), 11.66 (bs, 1H), 12.62 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 480 (M⁺+1)

Example 1147: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-phenylacetyl)thiourea

[1399] 2-Phenylethanoyl isothiocyanate was prepared using commercially available 2-phenylethanoyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-phenylethanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (41 mg, yield 53%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.88 (s, 2H), 3.94 (s, 3H), 3.96 (s, 3H), 6.41 (d, J = 5.12 Hz, 1H), 7.29 - 7.36 (m, 5H), 7.42 (s, 1H), 7.46 (d, J = 8.78 Hz, 1H), 7.52 (s, 1H), 7.66 - 7.69 (m, 1H), 8.11 - 8.14 (m, 1H), 8.51 (d, J = 5.12 Hz, 1H), 11.82 (s, 1H), 12.44 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 508 (M⁺+1)

Example 1148: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(2-phenylacetyl)thiourea

[1400] 2-Phenylethanoyl isothiocyanate was prepared using commercially available 2-phenylethanoyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-phenylethanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (38 mg, yield 48%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.66 (s, 2H), 3.97 (s, 3H), 3.99 (s, 3H), 7.23 - 7.34 (m, 10H), 7.55 (s, 1H), 7.69 (d, J = 9.03 Hz, 1H), 8.53 (s, 1H), 10.28 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 475 (M⁺+1)

Example 1149: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N-ethyl-N'-(2-phenylacetyl)thiourea

[1401] 2-Phenylethanoyl isothiocyanate was prepared using commercially available 2-phenylethanoyl chloride (80 mg) as a starting compound according to the description of the literature. N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N-ethylamine (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-phenylethanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (38 mg, yield 48%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.13 - 1.19 (m, 3H), 3.44 (bs, 2H), 3.94 (s, 3H), 3.96 (s, 3H), 4.19 (bs, 2H), 6.55 (d, J = 5.37 Hz, 1H), 7.06 - 7.11 (m, 3H), 7.19 - 7.34 (m, 6H), 7.42 (s, 1H), 7.47 (s, 1H), 8.53 (d, J = 5.12 Hz, 1H), 10.74 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

Example 1150: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-2-morpholinoaniline

[1402] 3-Fluoro-4-nitrophenol (300 mg), morpholine (800 μl), and calcium carbonate (50 mg) were added to dimethylformamide (3 ml), and the mixture was heated at 130°C for 12 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give 3-morpholino-4-nitrophenol (400 mg, yield 94%). The resultant 3-morpholino-4-nitrophenol (400 mg) was added to dimethylformamide (3 ml). Palladium hydroxid-carbon (110 mg) and hydrogen were added thereto, and the mixture was stirred at room temperature for 4 hr. The reaction solution was filtered through Celite, and the filtrate was concentrated. The residue was then purified by chromatography on silica gel using chloroform/acetone for development to give 4-amino-3-morpholinophenol (296 mg, yield 85%). The resultant 4-amino-3-morpholinophenol (296 mg), 4-chloro-6,7-dimethoxyquinazoline (479 mg), and n-tetraethylammonium bromide (244 mg) were dissolved in ethyl methyl ketone (10 ml) to prepare a solution. A solution (10 ml) of sodium hydroxide (479 mg) in water was added to the solution, and the mixture was stirred at 80°C for 4 hr. Water was added to the reaction solution, and the organic layer was extracted and was concentrated. The residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (396 mg, yield 68%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.59 - 3.61 (m, 4H), 3.76 - 3.81 (m, 4H), 3.92 (s, 3H), 3.93 (s, 3H), 7.16 (s, 2H), 7.23 (s, 2H), 8.52 (s, 2H)

Mass spectrometry value (ESI-MS, m/z): 383 (M⁺+1)

Example 1151: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-morpholinophenyl}-N'-(2-methylbenzoyl)thiourea

[1403] N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-2-morpholinoaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 2-methyl-1-benzenecarbonyl isothiocyanate (50 μ l) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (65 mg, yield 89%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.50 (s, 3H), 2.88 - 2.91 (m, 4H), 3.79 - 3.81 (m, 4H), 3.98 (s, 3H), 3.99 (s, 3H), 7.14 (d, J = 11.22 Hz, 1H), 7.18 (s, 1H), 7.33 (d, J = 9.76 Hz, 2H), 7.40 (s, 1H), 7.45 (t, J = 7.40 Hz, 1H), 7.54 (d, J = 7.56 Hz, 1H), 7.57 (s, 1H), 7.59 (s, 1H), 8.67 (d, J = 12.93 Hz, 1H), 11.76 (s, 1H), 13.09 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 560 (M⁺+1)

Example 1152: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-(3-pyridylcarbonyl)thiourea

[1404] 3-Pyridinecarbonyl isothiocyanate was prepared using commercially available 3-pyridinecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-pyridinecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (83 mg, yield 64%).

¹H-NMR (CDCl₃, 400 MHz): δ 3.95 (s, 3H), 4.06 (s, 3H), 6.57 (d, J = 5.12 Hz, 1H), 7.24 - 7.27 (m, 3H), 7.45 (s, 1H), 7.51 - 7.54 (m, 2H), 7.82 (d, J = 6.83 Hz, 2H), 8.21 - 8.24 (m, 1H), 8.53 (d, J = 5.12 Hz, 1H), 8.89 - 8.91 (m, 1H), 9.18 (d, J = 2.44 Hz, 1H), 9.22 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 461 (M⁺+1)

Example 1153: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-[4-(morpholinomethyl)benzoyl]thiourea

[1405] Commercially available 4-bromomethylbenzoic acid (300 mg) was dissolved in acetonitrile (10 ml). Potassium carbonate (30 mg) and morpholine (130 μ l) were added to the solution, and the mixture was stirred at room temperature for one hr. The reaction layer was subjected to separation with chloroform and a saturated aqueous sodium hydrogen-carbonate solution. The organic layer was then concentrated to give methyl 4-(morpholinomethyl)benzoate. Methanol (1 ml), water (150 μ l), and potassium hydroxide (15 mg) were added to the residue, and the mixture was heated at 60°C for one hr. After the completion of the reaction, the solvent was removed by distillation to give 4-(morpholinomethyl)benzoic acid. Toluene (20 ml) and thionyl chloride (1 ml) were added to the residue, and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-(morpholinomethyl)-1-benzenecarbonyl isothiocyanate was prepared using the resultant 4-(morpholinomethyl)-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-(morpholinomethyl)-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (74 mg, yield 78%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.47 (s, 4H), 3.59 (s, 2H), 3.72 - 3.75 (m, 4H), 4.07 (s, 3H), 4.08 (s, 3H), 7.27 (s, 2H), 7.32 - 7.34 (m, 3H), 7.53 - 7.56 (m, 3H), 7.85 - 7.88 (m, 4H), 8.64 (s, 1H), 9.12 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 559 (M⁺+1)

Example 1154: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[(6-methyl-3-pyridyl)carbonyl]thiourea

[1406] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 6-methylnicotinic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 6-methyl-3-pyridinecarbonyl isothiocyanate was prepared using the resultant 6-methyl-3-pyridinecarbonyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 6-methyl-3-pyridinecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (71 mg, yield 89%).

¹H-NMR (CDCl₃, 400 MHz): δ 2.58 (s, 3H), 3.97 (s, 3H), 3.99 (s, 3H), 7.37 - 7.40 (m, 3H), 7.46 (d, J = 8.29 Hz, 1H), 7.58 (s, 1H), 7.79 (d, J = 8.78 Hz, 2H), 8.26 (dd, J = 2.44 Hz, J = 8.05 Hz, 1H), 8.59 (s, 1H), 9.00 (d, J = 2.19 Hz, 1H), 11.82 (bs, 1H), 12.52 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 476 ($M^+ + 1$)

Example 1155: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(4-pyridylcarbonyl)thiourea

[1407] 4-Pyridinecarbonyl isothiocyanate was prepared using commercially available 4-pyridinecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-pyridinecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (73 mg, yield 94%).

$^1\text{H-NMR}$ (DMSO- d_6 , 400 MHz): δ 3.98 (s, 3H), 3.99 (s, 3H), 7.37 - 7.40 (m, 3H), 7.58 (s, 1H), 7.79 (d, J = 8.78 Hz, 2H), 7.87 (d, J = 6.09 Hz, 2H), 8.58 (s, 1H), 8.79 (d, J = 6.09 Hz, 2H), 11.89 (bs, 1H), 12.34 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 462 ($M^+ + 1$)

Example 1156: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(2-pyridylcarbonyl)thiourea

[1408] 2-Pyridinecarbonyl isothiocyanate was prepared using commercially available 2-pyridinecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-pyridinecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (69 mg, yield 90%).

$^1\text{H-NMR}$ (DMSO- d_6 , 400 MHz): δ 3.98 (s, 3H), 3.99 (s, 3H), 7.39 - 7.42 (m, 3H), 7.58 (s, 1H), 7.81 - 7.84 (m, 3H), 8.16 - 8.20 (m, 1H), 8.28 (d, J = 7.56 Hz, 1H), 8.58 (s, 1H), 8.82 (d, J = 4.64 Hz, 1H), 10.85 (bs, 1H), 12.18 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 462 ($M^+ + 1$)

Example 1157: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[2-(trifluoromethyl)benzoyl]thiourea

[1409] 2-(Trifluoromethyl)-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-(trifluoromethyl)-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-(trifluoromethyl)-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (49 mg, yield 56%).

$^1\text{H-NMR}$ (DMSO- d_6 , 400 MHz): δ 3.99 (s, 3H), 4.02 (s, 3H), 7.38 - 7.40 (m, 2H), 7.59 (s, 1H), 7.76 - 7.88 (m, 7H), 8.58 (s, 1H), 12.14 (bs, 1H), 12.29 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 529 ($M^+ + 1$)

Example 1158: N-(3,5-Dichlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}thiourea

[1410] 3,5-Dichloro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3,5-dichloro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3,5-dichloro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (40 mg, yield 45%).

$^1\text{H-NMR}$ (DMSO- d_6 , 400 MHz): δ 3.98 (s, 3H), 3.99 (s, 3H), 7.37 - 7.40 (m, 4H), 7.58 (s, 1H), 7.67 (bs, 1H), 7.76 - 7.81 (m, 1H), 7.88 (s, 1H), 7.94 (s, 1H), 8.00 (s, 1H), 8.17 (bs, 1H), 8.58 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 530 ($M^+ + 1$)

Example 1159: N-{2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(3,5-dichlorobenzoyl)thiourea

[1411] 3,5-Dichloro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3,5-dichloro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3,5-dichloro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the

mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (40 mg, yield 47%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.93 (s, 3H), 3.96 (s, 3H), 6.66 (d, J = 4.88 Hz, 1H), 7.43 (s, 1H), 7.48 (s, 1H), 7.61 (s, 1H), 7.67 (s, 1H), 7.79 (s, 1H), 7.94 - 8.17 (m, 3H), 8.57 (d, J = 5.12 Hz, 1H), 12.09 (bs, 1H), 12.42 (bs, 1H)
Mass spectrometry value (ESI-MS, m/z): 563 (M⁺+1)

Example 1160: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]-3-fluorophenyl}-N'-(2-fluorobenzoyl)thiourea

[1412] 2-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2-fluoroaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-fluoro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (68 mg, yield 86%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 6.52 (d, J = 4.88 Hz, 1H), 7.35 - 7.40 (m, 2H), 7.43 (s, 1H), 7.50 - 7.55 (m, 2H), 7.61 - 7.73 (m, 2H), 7.75 (t, J = 5.85 Hz, 1H), 8.07 (d, J = 11.95 Hz, 1H), 8.52 (d, J = 5.37 Hz, 1H), 11.85 (s, 1H), 12.43 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 496 (M⁺+1)

Example 1161: N-{4-[(6,7-Dimethoxy-4-quinazolinyloxy)phenyl]-N'-(2-fluorobenzoyl)thiourea

[1413] 2-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-fluoro-1-benzenecarbonyl isothiocyanate (50 μl) in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (43 mg, yield 53%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.98 (s, 3H), 3.99 (s, 3H), 7.34 - 7.40 (m, 5H), 7.58 (s, 1H), 7.60 - 7.79 (m, 4H), 8.58 (s, 1H), 11.74 (s, 1H), 12.32 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 479 (M⁺+1)

Example 1162: N-(2,6-Dichlorobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyloxy)phenyl]thiourea

[1414] 2,6-Dichloro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,6-dichloro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyloxy)aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2,6-dichloro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (56 mg, yield 63%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.98 (s, 3H), 3.99 (s, 3H), 7.39 (d, J = 10.73 Hz, 3H), 7.47 - 7.61 (m, 4H), 7.79 (d, J = 8.78 Hz, 2H), 8.59 (s, 1H), 12.22 (bs, 1H), 12.35 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 530 (M⁺+1)

Example 1163: N-{2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(3-fluorobenzoyl)thiourea

[1415] 3-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-fluoro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (50 mg, yield 58%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.92 (s, 3H), 3.93 (s, 3H), 6.66 (d, J = 5.12 Hz, 1H), 7.20 (s, 1H), 7.32 - 7.36 (m, 1H), 7.43 (s, 1H), 7.48 (s, 1H), 7.60 - 7.62 (m, 2H), 7.86 (d, J = 9.03 Hz, 1H), 8.56 (d, J = 5.12 Hz, 1H), 11.95 (bs, 1H), 12.55 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 512 (M⁺+1)

Example 1164: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(3-fluorobenzoyl)thiourea

[1416] 3-Fluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-fluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-fluoro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (60 mg, yield 75%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.98 (s, 3H), 3.99 (s, 3H), 7.37 - 7.40 (m, 3H), 7.52 - 7.55 (m, 1H), 7.58 - 7.61 (m, 2H), 7.78 - 7.86 (m, 4H), 8.58 (s, 1H), 12.05 (bs, 1H), 12.43 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 479 (M⁺+1)

Example 1165: N-(3-Bromobenzoyl)-N'-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1417] 3-Bromo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3-bromo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3-bromo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (56 mg, yield 58%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.46 (s, 3H), 3.92 (s, 3H), 6.61 (d, J = 5.37 Hz, 1H), 7.19 - 7.22 (m, 1H), 7.32 - 7.36 (m, 1H), 7.48 (s, 1H), 7.52 (t, J = 7.93 Hz, 1H), 7.61 (d, J = 2.68 Hz, 1H), 7.88 (d, J = 8.05 Hz, 1H), 7.99 (d, J = 8.05 Hz, 1H), 8.09 (d, J = 9.06 Hz, 1H), 8.21 (s, 1H), 8.56 (d, J = 5.12 Hz, 1H), 12.02 (bs, 1H), 12.53 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 573 (M⁺+1)

Example 1166: N-(4-Bromobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1418] 4-Bromo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-bromo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-bromo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (57 mg, yield 63%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.93 (s, 3H), 3.96 (s, 3H), 6.55 (d, J = 5.12 Hz, 1H), 7.33 (d, J = 8.78 Hz, 2H), 7.41 (s, 1H), 7.51 (s, 1H), 7.77 (d, J = 8.78 Hz, 2H), 7.82 (d, J = 8.78 Hz, 2H), 7.93 (d, J = 8.54 Hz, 2H), 8.52 (d, J = 5.37 Hz, 1H), 11.65 (bs, 1H), 12.47 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 539 (M⁺+1)

Example 1167: N-(4-Bromobenzoyl)-N'-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1419] 4-Bromo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-bromo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-bromo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (46 mg, yield 53%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.92 (s, 3H), 3.93 (s, 3H), 6.66 (d, J = 5.12 Hz, 1H), 7.20 (s, 1H), 7.32 - 7.36 (m, 1H), 7.43 (s, 1H), 7.48 (s, 1H), 7.60 (d, J = 2.68 Hz, 1H), 7.78 (d, J = 8.78 Hz, 1H), 7.95 (d, J = 8.78 Hz, 1H), 8.56 (d, J = 5.12 Hz, 1H), 11.96 (bs, 1H), 12.57 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 573 (M⁺+1)

Example 1168: N-(4-Bromobenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}thiourea

[1420] 4-Bromo-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-bromo-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-bromo-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chroma-

tography on silica gel using chloroform/acetone for development to give the title compound (53 mg, yield 58%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.98 (s, 3H), 3.99 (s, 3H), 7.37 - 7.40 (m, 3H), 7.58 (s, 1H), 7.76 - 7.92 (m, 4H), 7.94 (d, J = 6.59 Hz, 2H), 8.58 (s, 1H), 11.72 (bs, 1H), 12.52 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 541 (M⁺+1)

Example 1169: N-{2-[4-(Bromomethyl)phenyl]acetyl}-N'-{4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1421] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-(bromomethyl)benzoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-[4-(bromomethyl)phenyl]ethanoyl isothiocyanate was prepared using the resultant 4-(bromomethyl)-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-[4-(bromomethyl)phenyl]ethanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (50 mg, yield 52%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.85 (s, 2H), 3.92 (s, 3H), 3.95 (s, 3H), 4.36 (s, 2H), 6.55 (d, J = 5.12 Hz, 1H), 7.29 (d, J = 9.03 Hz, 2H), 7.30 - 7.41 (m, 5H), 7.49 (s, 1H), 7.75 (d, J = 8.78 Hz, 2H), 8.29 (d, J = 5.37 Hz, 1H), 11.75 (bs, 1H), 12.39 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) 567 (M⁺+1)

Example 1170: N-(5-Chloropentanoyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}thiourea

[1422] 5-Chloropentanoyl isothiocyanate was prepared using commercially available 5-chloropentanoyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 5-chloropentanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (46 mg, yield 58%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.49 - 2.55 (m, 6H), 3.36 - 3.69 (m, 2H), 3.93 (s, 3H), 3.96 (s, 3H), 7.34 - 7.39 (m, 3H), 7.58 (s, 1H), 7.73 (d, J = 9.03 Hz, 2H), 8.58 (s, 1H), 11.49 (s, 1H), 12.50 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 475 (M⁺+1)

Example 1171: N-{4-[(6,7-Dimethoxy-4-quinolyl)oxy]phenyl}-N'-[2-(2-thienyl)acetyl]thiourea

[1423] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-thienyl)acetic acid (40 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-thienyl)ethanoyl isothiocyanate was prepared using the resultant 2-(2-thienyl)ethanoyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-(2-thienyl)ethanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (44 mg, yield 54%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.96 (s, 3H), 3.98 (s, 3H), 4.07 (s, 2H), 6.64 (d, J = 5.61 Hz, 1H), 6.96 - 7.03 (m, 6H), 7.33 - 7.38 (m, 1H), 7.45 (s, 1H), 7.78 (d, J = 9.03 Hz, 1H), 8.61 (d, J = 5.37 Hz, 1H), 11.75 (bs, 1H), 12.34 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 480 (M⁺+1)

Example 1172: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[2-(2-thienyl)acetyl]thiourea

[1424] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-(2-thienyl)acetic acid (40 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-(2-thienyl)ethanoyl isothiocyanate was prepared using the resultant 2-(2-thienyl)ethanoyl chloride as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-(2-thienyl)ethanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (46 mg, yield 57%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.79 (s, 6H), 3.98 (d, J = 6.34 Hz, 2H), 6.68 (d, J = 9.03 Hz, 2H), 6.96 - 7.00

(m, 3H), 7.34 - 7.39 (m, 5H), 9.19 (s, 1H), 9.92 (bs, 1H)
Mass spectrometry value (ESI-MS, m/z): 481 (M⁺+1)

Example 1173: N-{2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(4-methoxybenzoyl)thiourea

[1425] 4-Methoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 4-methoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-methoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (36 mg, yield 46%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.92 (s, 9H), 7.09 (d, J = 8.78 Hz, 1H), 7.19 - 7.22 (m, 3H), 7.31 - 7.36 (m, 2H), 7.43 (s, 1H), 7.48 (s, 1H), 8.06 (d, J = 8.78 Hz, 1H), 8.12 (d, J = 9.03 Hz, 1H), 8.53 - 8.57 (m, 1H), 11.52 (bs, 1H), 12.55 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z) : 525 (M⁺+1)

Example 1174: N-(4-Chlorobenzoyl)-N'-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1426] 2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. Commercially available 4-chloro-1-benzenecarbonyl isothiocyanate was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (49 mg, yield 61%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.92 (s, 3H), 3.93 (s, 3H), 6.66 (d, J = 5.12 Hz, 1H), 7.19 - 7.21 (m, 2H), 7.32 - 7.36 (m, 1H), 7.43 (s, 1H), 7.47 (s, 1H), 7.48 (s, 1H), 7.63 (d, J = 8.78 Hz, 1H), 8.03 (d, J = 8.78 Hz, 2H), 8.57 (d, J = 5.12 Hz, 1H), 11.96 (bs, 1H), 12.57 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 529 (M⁺+1)

Example 1175: N-(2,4-Dimethoxybenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}thiourea

[1427] 2,4-Dimethoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-dimethoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2,4-dimethoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (51 mg, yield 58%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.90 (s, 3H), 3.98 (s, 3H), 3.99 (s, 3H), 4.07 (s, 3H), 6.79 - 6.81 (m, 2H), 7.37 - 7.40 (m, 3H), 7.58 (s, 1H), 7.79 - 7.81 (m, 2H), 8.00 (d, J = 9.03 Hz, 1H), 8.58 (s, 1H), 11.01 (bs, 1H), 12.68 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 521 (M⁺+1)

Example 1176: N-{2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2,4-dimethoxybenzoyl)thiourea

[1428] 2,4-Dimethoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-dimethoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Chloro-4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2,4-dimethoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (40 mg, yield 48%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.93 (s, 3H), 3.96 (s, 3H), 4.05 (s, 3H), 4.06 (s, 3H), 6.66 (d, J = 5.12 Hz, 1H), 6.78 - 6.81 (m, 2H), 7.36 (s, 1H), 7.43 (s, 1H), 7.48 (s, 1H), 7.61 (s, 1H), 8.01 (d, J = 8.54 Hz, 1H), 8.19 (d, J = 9.03 Hz, 1H), 8.56 (d, J = 5.12 Hz, 1H), 11.18 (bs, 1H), 12.67 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 555 (M⁺+1)

Example 1177: Ethyl 5-[(4-[(6,7-dimethoxy-4-quinazolinyl)oxy]anilino)carbothioyl]amino]-5-oxopentanoate

[1429] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 5-ethoxy-5-oxopentanoic acid (40 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and ethyl 5-isothiocyanat-5-oxopentanoate was prepared using the resultant ethyl 5-chloro-5-oxopentanoate as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of ethyl 5-isothiocyanat-5-oxopentanoate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (39 mg, yield 47%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.16 - 1.22 (m, 3H), 1.78 - 1.91 (m, 2H), 2.32 - 2.47 (m, 2H), 2.48 - 2.54 (m, 2H), 3.92 (s, 3H), 3.95 (s, 3H), 4.03 - 4.09 (m, 2H), 6.76 (d, J = 8.78 Hz, 1H), 7.29 - 7.39 (m, 4H), 7.52 (s, 1H), 7.73 (d, J = 5.37 Hz, 1H), 11.49 (s, 1H), 12.47 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 499 (M⁺+1)

Example 1178: Ethyl 4-[(4-[(6,7-dimethoxy-4-quinazolinyl)oxy]anilino)carbothioyl]amino]-4-oxobutanoate

[1430] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-ethoxy-5-oxobutanoic acid (40 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and ethyl 4-isothiocyanat-4-oxobutanoate was prepared using the resultant ethyl 4-chloro-4-oxobutanoate as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of ethyl 4-isothiocyanat-4-oxobutanoate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (38 mg, yield 47%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.16 - 1.24 (m, 3H), 2.51 - 2.63 (m, 2H), 2.73 - 2.78 (m, 2H), 3.92 (s, 3H), 3.95 (s, 3H), 4.02 - 4.11 (m, 2H), 7.29 - 7.39 (m, 3H), 7.57 (s, 1H), 7.70 - 7.74 (m, 2H), 8.62 (s, 1H), 11.60 (s, 1H), 12.38 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 485 (M⁺+1)

Example 1179: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-cyclohexylcarbonylthiourea

[1431] 1-Cyclohexanecarbonyl isothiocyanate was prepared using commercially available 1-cyclohexanecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 1-Cyclohexanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (44 mg, yield 58%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.16 - 1.41 (m, 6H), 1.66 - 1.85 (m, 4H), 2.55 - 2.61 (m, 1H), 3.94 (s, 3H), 3.95 (s, 3H), 6.41 (d, J = 5.1 Hz, 1H), 7.42 (s, 1H), 7.46 (d, J = 8.8 Hz, 1H), 7.52 (s, 1H), 7.68 (dd, J = 2.2 Hz, 8.5 Hz, 1H), 8.15 (d, J = 2.2 Hz, 1H), 8.50 (d, J = 5.1 Hz, 1H), 11.51 (s, 1H), 12.59 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 500 (M⁺+1)

Example 1180: N-Cyclohexylcarbonyl-N'-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]thiourea

[1432] 1-Cyclohexanecarbonyl isothiocyanate was prepared using commercially available 1-cyclohexanecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 1-Cyclohexanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (48 mg, yield 62%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.16 - 1.45 (m, 6H), 1.66 - 1.86 (m, 4H), 2.55 - 2.61 (m, 1H), 3.98 (s, 3H), 3.99 (s, 3H), 7.34 (d, J = 15.6 Hz, 2H), 7.39 (s, 1H), 7.56 (s, 1H), 7.73 (d, J = 9.0 Hz, 2H), 8.56 (s, 1H), 11.41 (s, 1H), 12.55 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 467 (M⁺+1)

Example 1181: N-Cyclopropylcarbonyl-N'-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]thiourea

[1433] 1-Cyclopropanecarbonyl isothiocyanate was prepared using commercially available 1-cyclopropanecarbonyl

chloride (80 mg) as a starting compound according to the description of the literature. 1-Cyclopropanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (51 mg, yield 71%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.95 - 0.99 (m, 4H), 2.10 - 2.14 (m, 1H), 3.98 (s, 3H), 3.99 (s, 3H), 7.34 (d, J = 9.0 Hz, 2H), 7.39 (s, 1H), 7.56 (s, 1H), 7.71 (d, J = 8.8 Hz, 2H), 8.56 (s, 1H), 11.81 (s, 1H), 12.53 (s, 1H)

Mass spectrometry value (ESI-MS, m/z)

Example 1182: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-cyclopentylcarbonylthiourea

[1434] 1-Cyclopentanecarbonyl isothiocyanate was prepared using commercially available 1-cyclopentanecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 1-Cyclopentanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (38 mg, yield 52%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.56 - 1.76 (m, 6H), 1.88 - 1.90 (m, 2H), 2.97 - 3.03 (m, 1H), 3.94 (s, 3H), 3.96 (s, 3H), 6.40 (d, J = 5.1 Hz, 1H), 7.42 (s, 1H), 7.46 (d, J = 8.8 Hz, 1H), 7.52 (s, 1H), 7.68 (dd, J = 2.7 Hz, 8.8 Hz, 1H), 8.15 (d, J = 2.4 Hz, 1H), 8.50 (d, J = 5.4 Hz, 1H), 11.56 (s, 1H), 12.60 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 486 (M⁺+1)

Example 1183: N-Cyclopentylcarbonyl-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}thiourea

[1435] 1-Cyclopentanecarbonyl isothiocyanate was prepared using commercially available 1-cyclopentanecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 1-Cyclopentanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by thin-layer chromatography using chloroform/acetone for development to give the title compound (24 mg, yield 31%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.55 - 1.90 (m, 8H), 2.99 - 3.03 (m, 1H), 3.98 (s, 3H), 3.99 (s, 3H), 7.34 (d, J = 8.8 Hz, 2H), 7.39 (s, 1H), 7.57 (s, 1H), 7.73 (d, J = 8.8 Hz, 2H), 8.56 (s, 1H), 11.47 (s, 1H), 12.56 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 453 (M⁺+1)

Example 1184: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-[3-(3-methylphenyl)propanoyl]thiourea

[1436] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-(3-methylphenyl)propanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-(3-methylphenyl)propanoyl isothiocyanate was prepared using the resultant 3-(3-methylphenyl)propanoyl chloride as a starting compound according to the description of the literature. 3-(3-Methylphenyl)propanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (31 mg, yield 38%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.29 (s, 3H), 2.77 - 2.89 (m, 4H), 3.94 (s, 3H), 3.96 (s, 3H), 6.41 (d, J = 5.4 Hz, 1H), 7.01 - 7.08 (m, 3H), 7.19 (t, J = 7.6 Hz, 1H), 7.42 (s, 1H), 7.47 (d, J = 8.8 Hz, 1H), 7.53 (s, 1H), 7.67 (dd, J = 2.4 Hz, 8.5 Hz, 1H), 8.13 (d, J = 2.7 Hz, 1H), 8.50 (d, J = 5.1 Hz, 1H), 11.62 (s, 1H), 12.53 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 537 (M⁺+1)

Example 1185: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[3-(3-methylphenyl)propanoyl]thiourea

[1437] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 3-(3-methylphenyl)propanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 3-(3-methylphenyl)propanoyl isothiocyanate was prepared using the resultant 3-(3-methylphenyl)propanoyl chloride as a starting compound according to the description of the literature. 3-(3-Methylphenyl)propanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by thin-layer chromatography using chloroform/acetone for

development to give the title compound (32 mg, yield 38%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.29 (s, 3H), 2.77 - 2.87 (m, 4H), 3.98 (s, 3H), 3.99 (s, 3H), 7.01 - 7.08 (m, 3H), 7.19 (t, J = 7.6 Hz, 1H), 7.34 (d, J = 8.8 Hz, 2H), 7.39 (s, 1H), 7.57 (s, 1H), 7.72 (d, J = 8.8 Hz, 2H), 8.56 (s, 1H), 11.52 (s, 1H), 12.50 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 503 (M⁺+1)

Example 1186: N-(4-Chlorobutanoyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}thiourea

[1438] 4-Chlorobutanoyl isothiocyanate was prepared using commercially available 4-chlorobutanoyl chloride (80 mg) as a starting compound according to the description of the literature. 4-Chlorobutanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by thin-layer chromatography using chloroform/acetone for development to give the title compound (30 mg, yield 38%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.04 (t, J = 6.8 Hz, 2H), 2.65 (t, J = 7.3 Hz, 2H), 3.70 (t, J = 6.6 Hz, 2H), 3.98 (s, 3H), 3.99 (s, 3H), 7.35 (d, J = 8.8 Hz, 2H), 7.39 (s, 1H), 7.57 (s, 1H), 7.72 (d, J = 8.8 Hz, 2H), 8.56 (s, 1H), 11.55 (s, 1H), 12.45 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 461 (M⁺+1)

Example 1187: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2,2-dimethylpropanoyl)thiourea

[1439] 2,2-Dimethylpropanoyl isothiocyanate was prepared using commercially available 2,2-dimethylpropanoyl chloride (80 mg) as a starting compound according to the description of the literature. 2,2-Dimethylpropanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by thin-layer chromatography using chloroform/acetone for development to give the title compound (31 mg, yield 43%).

¹H-NMR (DMSO-d₆, 400 MHz): 1.27 (s, 9H), 3.94 (s, 3H), 3.96 (s, 3H), 6.41 (d, J = 5.1 Hz, 1H), 7.42 (s, 1H), 7.47 (d, J = 8.8 Hz, 1H), 7.52 (s, 1H), 7.68 (dd, J = 2.4 Hz, 8.8 Hz, 1H), 8.12 (s, 1H), 8.51 (d, J = 5.1 Hz, 1H), 10.78 (s, 1H), 12.50 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 474 (M⁺+1)

Example 1188: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(2,2-dimethylpropanoyl)thiourea

[1440] 2,2-Dimethylpropanoyl isothiocyanate was prepared using commercially available 2,2-dimethylpropanoyl chloride (80 mg) as a starting compound according to the description of the literature. 2,2-Dimethylpropanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by thin-layer chromatography using chloroform/acetone for development to give the title compound (43 mg, yield 58%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.28 (s, 9H), 3.98 (s, 3H), 3.99 (s, 3H), 7.35 (d, J = 8.8 Hz, 2H), 7.39 (s, 1H), 7.57 (s, 1H), 7.72 (d, J = 8.5 Hz, 2H), 8.57 (s, 1H), 10.66 (s, 1H), 12.59 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 441 (M⁺+1)

Example 1189: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-hexanoylthiourea

[1441] Hexanoyl isothiocyanate was prepared using commercially available hexanoyl chloride (80 mg) as a starting compound according to the description of the literature. Hexanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by thin-layer chromatography using chloroform/acetone for development to give the title compound (10 mg, yield 13%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.84 - 0.91 (m, 3H), 1.22 - 1.32 (m, 4H), 1.45 - 1.64 (m, 2H), 2.18 (t, J = 7.3 Hz, 2H), 3.98 (s, 3H), 3.99 (s, 3H), 7.33 - 7.37 (m, 2H), 7.39 (s, 1H), 7.57 (s, 1H), 7.70 - 7.75 (m, 2H), 8.56 (s, 1H), 11.45 (s, 1H), 12.59 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 455 (M⁺+1)

Example 1190: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-[(2-methylcyclopropyl)carbonyl]thiourea

[1442] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-methyl-1-cyclopropanecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-methyl-1-cyclopropanecarbonyl isothiocyanate was prepared using the resultant 2-methyl-1-cyclopropanecarbonyl chloride as a starting compound according to the description of the literature. 2-Methyl-1-cyclopropanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (40 mg, yield 56%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.84 - 0.89 (m, 1H), 1.08 - 1.38 (m, 5H), 1.87 - 1.91 (m, 1H), 3.94 (s, 3H), 3.95 (s, 3H), 6.40 (d, J = 5.1 Hz, 1H), 7.42 (s, 1H), 7.46 (d, J = 8.8 Hz, 1H), 7.52 (s, 1H), 7.66 (dd, J = 2.7 Hz, 8.8 Hz, 1H), 8.13 (d, J = 2.4 Hz, 1H), 8.49 (d, J = 5.4 Hz, 1H), 11.82 (s, 1H), 12.58 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 472 (M⁺+1)

Example 1191: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[(2-methylcyclopropyl)carbonyl]thiourea

[1443] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-methyl-1-cyclopropanecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-methyl-1-cyclopropanecarbonyl isothiocyanate was prepared using the resultant 2-methyl-1-cyclopropanecarbonyl chloride as a starting compound according to the description of the literature. 2-Methyl-1-cyclopropanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (13 mg, yield 18%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.84 - 0.88 (m, 1H), 1.09 - 1.24 (m, 5H), 1.88 - 1.90 (m, 1H), 3.98 (s, 3H), 3.99 (s, 3H), 7.33 (d, J = 9.0 Hz, 2H), 7.39 (s, 1H), 7.56 (s, 1H), 7.71 (d, J = 9.0 Hz, 2H), 8.56 (s, 1H), 11.73 (s, 1H), 12.54 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 439 (M⁺+1)

Example 1192: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-[(1-methylcyclohexyl)carbonyl]thiourea

[1444] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 1-methyl-1-cyclohexanecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 1-methyl-1-cyclohexanecarbonyl isothiocyanate was prepared using the resultant 1-methyl-1-cyclohexanecarbonyl chloride as a starting compound according to the description of the literature. 1-Methyl-1-cyclohexanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (38 mg, yield 49%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.26 (s, 3H), 1.35 - 1.52 (m, 8H), 2.06 - 2.09 (m, 2H), 3.94 (s, 3H), 3.96 (s, 3H), 6.41 (d, J = 5.1 Hz, 1H), 7.42 (s, 1H), 7.47 (d, J = 8.8 Hz, 1H), 7.52 (s, 1H), 7.68 - 7.72 (m, 1H), 8.15 (s, 1H), 8.50 (d, J = 5.1 Hz, 1H), 10.66 (s, 1H), 12.65 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 515 (M⁺+1)

Example 1193: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[(1-methylcyclohexyl)carbonyl]thiourea

[1445] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 1-methyl-1-cyclohexanecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 1-methyl-1-cyclohexanecarbonyl isothiocyanate was prepared using the resultant 1-methyl-1-cyclohexanecarbonyl chloride as a starting compound according to the description of the literature. 1-Methyl-1-cyclohexanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (31 mg, yield 38%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.26 (s, 3H), 1.38 - 1.52 (m, 8H), 2.05 - 2.11 (m, 2H), 3.98 (s, 3H), 3.99 (s, 3H), 7.35 (d, J = 8.8 Hz, 2H), 7.39 (s, 1H), 7.57 (s, 1H), 7.74 (d, J = 8.8 Hz, 2H), 8.57 (s, 1H), 10.54 (s, 1H), 12.62 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 481 (M⁺+1)

Example 1194: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-[(1-phenylcyclopropyl)carbonyl]thiourea

[1446] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 1-phenyl-1-cyclopropanecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 1-phenyl-1-cyclopropanecarbonyl isothiocyanate was prepared using the resultant 1-phenyl-1-cyclopropanecarbonyl chloride as a starting compound according to the description of the literature. 1-Phenyl-1-cyclopropanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by thin-layer chromatography using chloroform/acetone for development to give the title compound (24 mg, yield 30%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.34 (s, 2H), 1.63 (s, 2H), 3.94 (s, 3H), 3.95 (s, 3H), 6.40 (d, J = 5.1 Hz, 1H), 7.42 - 7.55 (m, 7H), 7.66 (d, J = 8.5 Hz, 1H), 8.07 (s, 1H), 8.50 (d, J = 5.1 Hz, 1H), 9.22 (s, 1H), 12.28 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 534 (M⁺+1)

Example 1195: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[(1-phenylcyclopropyl)carbonyl]thiourea

[1447] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 1-phenyl-1-cyclopropanecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 1-phenyl-1-cyclopropanecarbonyl isothiocyanate was prepared using the resultant 1-phenyl-1-cyclopropanecarbonyl chloride as a starting compound according to the description of the literature. 1-Phenyl-1-cyclopropanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by thin-layer chromatography using chloroform/acetone for development to give the title compound (58 mg, yield 69%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 1.34 (s, 2H), 1.64 (s, 2H), 3.97 (s, 3H), 3.99 (s, 3H), 7.32 - 7.55 (m, 8H), 7.69 (d, J = 7.3 Hz, 2H), 8.55 (s, 1H), 9.00 (s, 1H), 12.25 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 501 (M⁺+1)

Example 1196: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-[(4-propylcyclohexyl)carbonyl]thiourea

[1448] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-propyl-1-cyclohexanecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-propyl-1-cyclohexanecarbonyl isothiocyanate was prepared using the resultant 4-propyl-1-cyclohexanecarbonyl chloride as a starting compound according to the description of the literature. 4-Propyl-1-cyclohexanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by thin-layer chromatography using chloroform/acetone for development to give the title compound (51 mg, yield 63%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.85 - 0.94 (m, 5H), 1.07 - 1.44 (m, 7H), 1.77 - 1.89 (m, 4H), 2.66 - 2.70 (m, 1H), 3.95 (s, 3H), 3.96 (s, 3H), 6.41 (d, J = 5.1 Hz, 1H), 7.43 (s, 1H), 7.47 (d, J = 8.8 Hz, 1H), 7.53 (s, 1H), 7.67 - 7.73 (m, 1H), 8.14 - 8.19 (m, 1H), 8.49 - 8.53 (m, 1H), 11.53 (s, 1H), 12.58 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 542 (M⁺+1)

Example 1197: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-[(4-propylcyclohexyl)carbonyl]thiourea

[1449] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-propyl-1-cyclohexanecarboxylic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-propyl-1-cyclohexanecarbonyl isothiocyanate was prepared using the resultant 4-propyl-1-cyclohexanecarbonyl chloride as a starting compound according to the description of the literature. 4-Propyl-1-cyclohexanecarbonyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by thin-layer chromatography using chloroform/acetone for development to give the title compound (59 mg, yield 69%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.85 - 0.91 (m, 5H), 1.15 - 1.41 (m, 7H), 1.78 - 1.89 (m, 4H), 2.66 - 2.69 (m, 1H), 3.98 (s, 3H), 3.99 (s, 3H), 7.35 (d, J = 6.6 Hz, 2H), 7.40 (s, 1H), 7.57 (s, 1H), 7.71 - 7.77 (m, 2H), 8.57 (s, 1H), 11.43 (s, 1H), 12.55 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 509 (M⁺+1)

Example 1198: N-(4-Chlorobutanoyl)-N'-{3-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}thiourea

[1450] 4-Chlorobutanoyl isothiocyanate was prepared using commercially available 4-chlorobutanoyl chloride (80 mg) as a starting compound according to the description of the literature. 4-Chlorobutanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (35 mg, yield 48%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.00 - 2.08 (m, 2H), 2.66 (t, J = 7.1 Hz, 2H), 3.71 (t, J = 6.6 Hz, 2H), 3.99 (s, 3H), 4.00 (s, 3H), 6.60 - 6.65 (m, 1H), 7.51 (s, 1H), 7.56 (d, J = 8.8 Hz, 1H), 7.64 (s, 1H), 7.73 - 7.78 (m, 1H), 8.18 - 8.23 (m, 1H), 8.67 (d, J = 5.6 Hz, 1H), 11.67 (s, 1H), 12.50 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 495 (M⁺+1)

Example 1199: N-(3-Chloropropanoyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}thiourea

[1451] 3-Chloropropanoyl isothiocyanate was prepared using commercially available 3-chloropropanoyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloropropanoyl isothiocyanate thus obtained was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (38 mg, yield 50%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.04 (t, J = 4.6 Hz, 2H), 3.88 (t, J = 3.7 Hz, 2H), 3.99 (s, 3H), 4.00 (s, 3H), 7.37 (d, J = 6.6 Hz, 2H), 7.40 (s, 1H), 7.58 (s, 1H), 7.73 (d, J = 6.3 Hz, 2H), 8.57 (s, 1H), 11.65 (s, 1H), 12.39 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 447 (M⁺+1)

Example 1200: N-{3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2-methylpentanoyl)thiourea

[1452] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 2-methylpentanoic acid (80 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 2-methylpentanoyl isothiocyanate was prepared using the resultant 2-methylpentanoyl chloride as a starting compound according to the description of the literature. The resultant 2-methylpentanoyl isothiocyanate was dissolved in ethanol (1 ml) to prepare a solution. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (69 mg, yield 94%).

¹H-NMR (chloroform-d, 400 MHz): δ 0.85 - 1.80 (m, 10H), 2.37 - 2.53 (m, 1H), 4.09 (s, 3H), 4.11 (s, 3H), 6.49 (d, J = 5.9 Hz, 1H), 7.31 (d, J = 5.1 Hz, 1H), 7.61 (s, 1H), 7.72 (dd, J = 2.4 Hz, 8.8 Hz, 1H), 7.76 (s, 1H), 8.08 (d, J = 2.4 Hz, 1H), 8.66 (s, 1H), 12.66 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 488 (M⁺+1)

Example 1201: N-{4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-(2-methylpentanoyl)thiourea

[1453] 2-Methylpentanoyl isothiocyanate prepared according to the method 2 was dissolved in ethanol (1 ml) to prepare a solution. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg), toluene (5 ml), and ethanol (1 ml) were added to the solution, and the mixture was stirred at room temperature for 16 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (44 mg, yield 57%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.87 - 0.92 (m, 3H), 1.09 - 1.13 (m, 3H), 1.26 - 1.65 (m, 4H), 2.74 - 2.81 (m, 1H), 3.98 (s, 3H), 4.00 (s, 3H), 7.34 - 7.38 (m, 2H), 7.40 (s, 1H), 7.57 (s, 1H), 7.72 - 7.78 (m, 2H), 8.57 (s, 1H), 11.51 (s, 1H), 12.59 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 455 (M⁺+1)

Example 1202: N-{2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(2,4-difluorobenzoyl)thiourea

[1454] 2,4-Difluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-difluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2,4-difluoro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the

mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (42 mg, yield 53%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.93 (s, 3H), 3.96 (s, 3H), 6.66 (d, J = 5.12 Hz, 1H), 7.16 - 7.36 (m, 5H), 7.61 (s, 1H), 7.82 - 7.83 (m, 1H), 8.10 (d, J = 9.03 Hz, 1H), 8.56 (d, J = 5.12 Hz, 1H), 11.98 (bs, 1H), 12.33 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 530 (M⁺+1)

Example 1203: N-(3,4-Dimethoxybenzoyl)-N'-{4-[(6,7-dimethoxy-4-quinazolinyloxy]phenyl}thiourea

[1455] 3,4-Dimethoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3,4-dimethoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyloxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3,4-dimethoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (57 mg, yield 65%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.79 (s, 3H), 3.83 (s, 3H), 3.96 (s, 3H), 3.99 (s, 3H), 6.62 (d, J = 15.61 Hz, 2H), 6.92 (d, J = 15.61 Hz, 2H), 7.04 (d, J = 8.54 Hz, 1H), 7.38 (s, 1H), 7.44 (s, 1H), 7.52 (s, 1H), 7.56 (dd, J = 2.19 Hz, J = 8.30 Hz, 1H), 8.56 (s, 1H), 11.88 (bs, 1H), 12.50 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 521 (M⁺+1)

Example 1204: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(3,4-dimethoxybenzoyl)thiourea

[1456] 3,4-Dimethoxy-1-benzenecarbonyl isothiocyanate was prepared using commercially available 3,4-dimethoxy-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 3,4-dimethoxy-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (49 mg, yield 58%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.79 (s, 3H), 3.83 (s, 3H), 3.93 (s, 3H), 3.94 (s, 3H), 5.46 (bs, 1H), 6.29 (d, J = 15.37 Hz, 1H), 6.62 - 6.43 (m, 1H), 6.79 (s, 1H), 7.03 - 7.10 (m, 2H), 7.38 (s, 1H), 7.52 (s, 1H), 7.55 - 7.58 (m, 2H), 8.44 (d, J = 5.12 Hz, 1H), 12.63 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 555 (M⁺+1)

Example 1205: N-[2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2-phenylacetyl)thiourea

[1457] 2-Phenylethanoyl isothiocyanate was prepared using commercially available 2-phenylethanoyl chloride (80 mg) as a starting compound according to the description of the literature. 2-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-phenylethanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (48 mg, yield 62%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.85 (s, 3H), 3.93 (s, 3H), 3.95 (s, 3H), 6.64 (d, J = 5.08 Hz, 1H), 7.27 - 7.39 (m, 5H), 7.42 (s, 1H), 7.49 (s, 1H), 7.57 (s, 1H), 8.10 (d, J = 8.78 Hz, 1H), 8.55 (d, J = 5.38 Hz, 1H), 11.91 (bs, 1H), 12.39 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 508 (M⁺+1)

Example 1206: N-[4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylphenyl]-N'-(2-phenylacetyl)thiourea

[1458] 2-Phenylethanoyl isothiocyanate was prepared using commercially available 2-phenylethanoyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinolyl)oxy]-2,3-dimethylaniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2-phenylethanoyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (44 mg, yield 58%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 2.08 (s, 3H), 2.15 (s, 3H), 3.85 (s, 2H), 3.94 (s, 3H), 3.95 (s, 3H), 6.28 (d, J = 5.12 Hz, 1H), 7.08 (d, J = 8.54 Hz, 1H), 7.27 - 7.41 (m, 7H), 7.57 (s, 1H), 8.47 (d, J = 5.37 Hz, 1H), 11.75 (bs, 1H),

12.01 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 502 (M⁺+1)

Example 1207: N-(2,4-Dichlorobenzoyl)-N'-[4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl]thiourea

[1459] 2,4-Dichloro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-dichloro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2,4-dichloro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (65 mg, yield 73%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.97 (s, 3H), 3.99 (s, 3H), 7.38 (d, J = 11.22 Hz, 3H), 7.55 - 7.58 (m, 2H), 7.69 (d, J = 8.29 Hz, 1H), 7.76 - 7.78 (m, 3H), 8.57 (s, 1H), 12.04 (bs, 1H), 12.26 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 530 (M⁺+1)

Example 1208: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(2,4-difluorobenzoyl)thiourea

[1460] 2,4-Difluoro-1-benzenecarbonyl isothiocyanate was prepared using commercially available 2,4-difluoro-1-benzenecarbonyl chloride (80 mg) as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 2,4-difluoro-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (50 mg, yield 63%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 3.95 (s, 3H), 3.96 (s, 3H), 6.43 (d, J = 5.37 Hz, 1H), 7.24 - 7.29 (m, 1H), 7.43 - 7.55 (m, 3H), 7.75 (dd, J = 2.44 Hz, J = 8.78 Hz, 1H), 7.79 - 7.90 (m, 2H), 8.16 (bs, 1H), 8.52 (d, J = 5.12 Hz, 1H), 11.86 (bs, 1H), 12.32 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 530 (M⁺+1)

Example 1209: N-[3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl]-N'-(4-octylbenzoyl)thiourea

[1461] Toluene (20 ml) and thionyl chloride (1 ml) were added to commercially available 4-octylbenzoic acid (40 mg), and the mixture was heated at 100°C for one hr. The solvent was removed by distillation, and 4-octyl-1-benzenecarbonyl isothiocyanate was prepared using the resultant 4-octyl-1-benzenecarbonyl chloride as a starting compound according to the description of the literature. 3-Chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]aniline (50 mg) was dissolved in toluene (5 ml) and ethanol (1 ml) to prepare a solution. A solution of 4-octyl-1-benzenecarbonyl isothiocyanate in ethanol (1 ml) was then added to the solution, and the mixture was stirred at room temperature for 2 hr. The reaction solution was concentrated, and the residue was purified by chromatography on silica gel using chloroform/acetone for development to give the title compound (53 mg, yield 58%).

¹H-NMR (DMSO-d₆, 400 MHz): δ 0.84 - 0.87 (m, 4H), 1.60 (m, 2H), 2.09 (s, 2H), 2.50 (s, 7H), 2.65 - 2.69 (m, 2H), 3.94 (s, 3H), 5.46 (bs, 1H), 6.29 (d, J = 15.37 Hz, 1H), 6.42 (d, J = 5.12 Hz, 1H), 7.36 - 7.54 (m, 6H), 7.74 - 7.76 (m, 1H), 7.94 (d, J = 8.05 Hz, 2H), 8.19 (bs, 1H), 8.51 (d, J = 5.12 Hz, 1H), 11.61 (bs, 1H), 12.70 (bs, 1H)

Mass spectrometry value (ESI-MS, m/z): 607 (M⁺+1)

Example 1210: N-4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl-N'-(4-piperidinobutyl)urea

[1462] Piperidine (357 mg) was dissolved in acetonitrile (20 ml) to prepare a solution. Potassium carbonate (97 mg) was then added to the solution. 2-(4-Bromobutyl)-1,3-isoindolinedione (1 g) was further added thereto, and the mixture was stirred with heating under reflux for 10 hr. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and brine. The extract was then dried over sodium sulfate, was filtered, and was concentrated to give 850 mg of a mixture containing 2-(4-piperidinobutyl)-1,3-isoindolinedione. The mixture containing 2-(4-piperidinobutyl)-1,3-isoindolinedione (850 mg) thus obtained was dissolved in ethyl alcohol (10 ml) to prepare a solution. Hydrazine monohydrate (0.75 ml) was then added to the solution, and the mixture was stirred at room temperature for one hr. This solution was concentrated to give 980 mg of a mixture containing 4-piperidinobutylamine. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-nitroaniline (100 mg) was dissolved in chloroform (10 ml) to prepare a solution. Triethylamine (1 ml) was then added to the solution, and a solution of triphosgene (131 mg) in chloroform (5 ml) was further added thereto. The mixture was stirred at room temperature for 10 min. A solution of

the mixture containing 4-piperidinobutylamine (69 mg) in chloroform (5 ml) was then added thereto, and the mixture was stirred at room temperature for 30 min. Water was added to stop the reaction, the reaction solution was then extracted with chloroform, and the extract was dried over sodium sulfate. The extract was filtered and concentrated. The powder thus obtained was then filtered and washed with diethyl ether to give N-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl-N'-(4-piperidinobutyl)-urea (104 mg, yield 68%).

¹H-NMR (CDCl₃, 400 MHz): δ 1.54 (brs, 2H), 1.65 - 1.79 (m, 8H), 2.52 - 2.61 (m, 6H), 3.35 (t, J = 5.9 Hz, 2H), 4.075 (s, 3H), 4.080 (s, 3H), 7.00 (brs, 1H), 7.34 (s, 1H), 7.51 - 7.54 (m, 2H), 8.12 (d, J = 2.7 Hz, 1H), 8.61 (s, 1H), 8.76 (d, J = 9.5 Hz, 1H), 9.73 (s, 1H)

Mass spectrometry value (ESI-MS, m/z): 525 (M⁺+1)

Example 1211: N-4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl-N'-(4-piperidinopropyl)urea

[1463] Piperidine (357 mg) was dissolved in acetonitrile (20 ml) to prepare a solution. Potassium carbonate (97 mg) was then added to the solution. Further, 2-(3-bromopropyl)-1,3-isindolinedione (1 g) was added thereto, and the mixture was stirred with heating under reflux for 10 hr. Water was added to stop the reaction, and the reaction solution was then extracted with ethyl acetate, followed by washing with water and brine. The extract was then dried over sodium sulfate, was filtered, and was concentrated to give 850 mg of a mixture containing 2-(3-piperidinopropyl)-1,3-isindolinedione. The mixture containing 2-(3-piperidinopropyl)-1,3-isindolinedione (850 mg) thus obtained was dissolved in ethyl alcohol (10 ml) to prepare a solution. Hydrazine monohydrate (0.75 ml) was then added to the solution, and the mixture was stirred at room temperature for one hr. This solution was concentrated to give 980 mg of a mixture containing 3-piperidinobutylamine. 4-[(6,7-Dimethoxy-4-quinazolinyl)oxy]-2-nitroaniline (100 mg) was dissolved in chloroform (10 ml) to prepare a solution. Triethylamine (1 ml) was then added to the solution. A solution of triphosgene (131 mg) in chloroform (5 ml) was further added to the solution, and the mixture was stirred at room temperature for 10 min. A solution of the mixture containing 3-piperidinopropylamine (69 mg) in chloroform (5 ml) was then added thereto, and the mixture was stirred at room temperature for 30 min. Water was added to stop the reaction, and the reaction solution was then extracted with chloroform, followed by washing with sodium sulfate. The extract was then filtered and was concentrated to give a powder. The powder was then filtered and was washed with diethyl ether to give N-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl-N'-(3-piperidinopropyl)urea (104 mg, yield 68%).

¹H-NMR (CDCl₃, 400 MHz): δ 1.55 (brs, 2H), 1.65 - 1.80 (m, 6H), 2.50 - 2.62 (m, 6H), 3.37 (t, J = 5.9 Hz, 2H), 4.075 (s, 3H), 4.080 (s, 3H), 7.05 (brs, 1H), 7.35 (s, 1H), 7.50 - 7.55 (m, 2H), 8.10 (d, J = 2.7 Hz, 1H), 8.60 (s, 1H), 8.78 (d, J = 9.5 Hz, 1H), 9.75 (s, 1H)

Mass spectrometry value (ESI-MS, m/z) : 511 (M⁺+1)

Pharmacological Test Example 1: Measurement of inhibitory activity against PDGF-Rα phosphorylation by PDGF-AA stimulation using G292

[1464] G-292 human osteosarcoma cells (Dainippon Pharmaceutical Co. Ltd.) were cultured in a DMEM medium (Dainippon Pharmaceutical Co. Ltd.) containing 10% FBS within an incubator containing 5% carbon dioxide until 80% confluent, and the cells were planted at 3x10⁴ cells per well in 96-well flat-bottom plates in the same medium containing 0.1% FBS. After cultivation at 37°C overnight, a solution of a test compound in dimethyl sulfoxide was added to each well, and a reaction was allowed to proceed at 37°C for one hr.

[1465] After the reaction of the test compound, PDGF-AA (Upstate) was added to 50 ng/ml, and the cells were stimulated at 37°C for 5 min. Thereafter, the cells were solubilized and shaken at room temperature for 20 min.

[1466] This solubilized cell solution was transferred to a 96-well plate coated with anti-phosphotyrosine antibody PY-20, and a reaction was allowed to proceed at 4°C overnight. Anti-PDGF-Rα (c-20) (Santa Cruz) was added as a primary antibody, and a reaction was allowed to proceed for one hr. GAR (Anti-rabbit Ig, horseradish peroxidase, Amersham) was then added as a secondary antibody, and a reaction was allowed to proceed for one hr. Color development was carried out using a color development kit for peroxidase (Sumitomo Bakelite Co., Ltd.), and the absorbance was measured at 450 nm. The phosphorylation of PDGF-Rα in the presence of the test compound was measured by presuming a phosphorylation degree of the receptor in the presence of a ligand to be 100% and a phosphorylation degree of PDGF-Rα in the absence of a ligand to be 0%, and IC₅₀ was then determined.

Pharmacological Test Example 2: PDGF-R autophosphorylation inhibition screening (dot plotting)

[1467] Vascular smooth muscle cells (passage 5 to 10) collected from rat thoracic aorta by the explant method were planted at 8x10³ cells per well in 96-well plates, subject to a serum starvation state, and 24 hr after the plantation then assayed.

[1468] A test compound was added, and the mixture was incubated at 37°C for one hr. Thereafter, PDGF-BB was

added to 50 ng/ml, and the mixture was incubated for 5 min, followed by washing with cold PBS. Lysate buffer (20 μ l/well) was then added, SDS buffer (20 ml/well) was added thereto, and 2 μ l of the mixture was then spotted on a PDVF membrane.

[1469] Treatment was carried out with anti-mouse IgG which had been labelled with peroxidase after treatment with an anti-phosphotyrosine antibody, followed by development in an ECL color development kit (Amersham). Thereafter, the color intensity was quantitatively determined by image analysis.

[1470] The inhibitory activity IC_{50} of the test compound was calculated by presuming a color intensity with the addition of PDGF and without the addition of the test compound to be 0% inhibition and a color intensity without the test compound and PDGF to be 100% inhibition.

Pharmacological Test Example 3: Inhibitory activity against c-kit autophosphorylation

[1471] Mole (human megakaryocytic leukemia cell line) which had been arrested for 20 hr was seeded into 96 well plates at an amount of 2×10^5 per well. A solution of a test compound in DMSO was added, and a reaction was then allowed to proceed for one hr. Thereafter, the cells were stimulated by 50 ng/ml of h-SCF for 5 min, followed by replacement with lysate buffer to solubilize the cells.

[1472] Next, the solubilized cell sap was transferred to a 96-well plate with an anti-phosphotyrosine antibody (PY-20) previously immobilized thereon, and a reaction was allowed to proceed. Thereafter, the cells were reacted with an anti-c-kit antibody (c-19, Santa Cruz) as a primary antibody and were labelled with GAR (anti-rabbit IgG, horseradish peroxidase, Amersham) as a secondary antibody. Color development was then carried out in a peroxidase color development kit (Sumitomo Bakelite Co., Ltd.), and the absorbance was measured at a wavelength of 450 nm.

[1473] The c-kit autophosphorylation inhibitory activity of the test compound was measured by presuming c-kit autophosphorylation activity with the addition of DMSO in the absence of h-SCF to be 100% inhibition and c-kit autophosphorylation activity with the addition of DMSO in the presence of h-SCF to be 0% inhibition, and IC_{50} was then determined.

[1474] The results of Pharmacological Test Examples 1 to 3 were as follows. Values within parentheses indicates IC_{50} (nM). Figures within parentheses in > 100 () in PDGF(E) indicate inhibition (%) at 100 nM. Figures within parentheses in > 1000 () and -() indicate inhibition (%) at 1000 nM. Figures within parentheses in -() of c-kit indicate inhibition (%) at 1000 nM. The symbol > indicates that the inhibition at an indicated concentration is not more than 50%. The symbols < and << indicate that the inhibition at an indicated concentration is not less than 50%.

Example No.	PDGF(E)	PDGF(D)	c-kit
1	<10		52
2	17		422
3	<10		173
4	<10		133
5	24		336
6	<10		175
7	12		616
8	<<10		62
9	<10		45
10	11		106
11	<<10		36
12	11		389
13	<10		135
14	12		209
15	21		-(48)
16	<10		495
17	<10		57
18	22		93
19	<<10		41
20	<<10		109
21	<10		135
22	<10		186

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	23	<10		475
	24	<<10		129
	25	<10		566
	26	<<10		44
	27	<<10		76
10	28	<10		118
	29	27		121
	30	<10		<30
	31	<10		221
	32	16		227
15	33	23		362
	34	>100(45)		800
	35	<10		342
	36	>100 (34)		- (19)
	37	<<10		<30
20	38	<10		33
	39	<10		56
	40	<<10		55
	41	<10		185
	42	<10		73
25	43	<10		158
	44	19		328
	45	<10		91
	46	22		388
	47	<10		178
30	48	<10		162
	49	<10		185
	50	<10		50
	51	14		270
	52	<10		273
35	53	<10		480
	54	15		473
	55	<10		288
	56	11		774
	57	11		393
40	58	12		499
	59	57		-(33)
	60	<10		261
	61	10		-(32)
	62	13		70
45	63	16		211
	64	90		429
	65	<10		103
	66	50		353
	67	<10		342
50	68	13		294
	69	53		755
	70	<10		451
	71	38		-(34)

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	72	36		387
	73	28		235
	74	100		1000
	75	25		1000
	76	>100(37)		-(14)
10	77	<10		99
	78	16		129
	79	18		123
	80	12		137
	81	12		408
15	82	10		176
	83	16		253
	84	27		399
	85	<10		163
	86	13		842
20	87	<10		607
	88	19		-(45)
	89	14		-(35)
	90	<10		621
	91	14		-(20)
25	92	<10		677
	93	17		601
	94	31		-(31)
	95	16		962
	96	38		-(13)
30	97	<10		254
	98	<10		152
	99	21		394
	100	14		815
	101	12		-(27)
35	102	<10		217
	103	15		200
	104	25		590
	105	<10		252
	106	12		1000
40	107			372
	108			180
	109			412
	110			110
	111			750
45	112	16		214
	113	18		402
	114	65		602
	115	<10		387
	116	31		1000
50	117	26		759
	118	33		746
	119	>100		-(31)
	120	13		505

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	121	48		-(17)
	122	11		821
	123	<10		207
	124	42		-(39)
	125	<10		671
10	126	19		-(10)
	127	16		283
	128	26		375
	129	64		732
	130	<10		714
15	131	38		-(40)
	132	26		301
	133	26		206
	134	>100(49)		944
	135	18		475
20	136	43		-(7)
	137	<10		233
	138	17		74
	139	57		80
	140	<10		234
25	141	36		-(26)
	142	<10		<30
	143	<10		<30
	144	18		49
	145	<10		<30
30	146	11		32
	147	11		<30
	148	<10		<30
	149	19		49
	150	<10		38
35	151	12		32
	152	<10		<30
	153	<10		<30
	154	40		61
	155	14		41
40	156	>100(48)		33
	157	<10		35
	158	12		107
	159	52		147
	160	16		52
45	161	<10		178
	162	16		162
	163	<10		185
	164	12		50
	165	49		149
50	166	34		145
	167	45		370
	168	15		52
	169	<10		31

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	170	<10		34
	171	22		83
	172	17		74
	173	<<10		37
	174	<10		70
10	175	<<10		45
	176	20		<30
	177	19		<30
	178	>100		
	179	70		
15	180	63		
	181	>100		
	182	>100		
	183	35		706
	184	38		369
20	185	46		
	186	63		
	187	<10		561
	188	100		
	189	57		
25	190	>100		
	191	84		503
	192	56		
	193	57		
	194	91		715
30	195	66		
	196	49		
	197	93		
	198	21		1000
	199	35		807
35	200	31		329
	201	>100		
	202	10		610
	203	25		169
	204	28		79
40	205	78		
	206	13		80
	207	31		55
	208	18		53
	209	>100		
45	210	16		95
	211	17		43
	212	28		70
	213	21		61
	214	>30(6)		47
50	215	8		<30
	216		<3	19
	217		29	39
	218		88	123

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	219		27	<30
	220		47	77
	221		84	109
	222		45	101
	223		7	101
10	224		>100	147
	225		86	453
	226		11	72
	227		7	194
	228		10	71
15	229		18	47
	230	8		111
	231	1		86
	232	11		42
	233	8		52
20	234	10		46
	235	<3		57
	236	4		47
	237	6		42
	238	10		36
25	239	9		183
	240	17		248
	241	12		232
	242	21		192
	243	20		190
30	244	27		69
	245	16		408
	246	58		243
	247	3		40
	248	11		147
35	249	4		57
	250	4		184
	251	6		185
	252	6		111
	253	17		514
40	254	>100(27)		396
	255	>100(36)		309
	256	<3		15
	257	6		22
	258	3		178
45	259	34		184
	260	6		180
	261	4		44
	262	7		83
	263	10		329
50	264	42		486
	265	35		122
	266		6	34
	267		23	35

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	268		6	34
	269	17		-(48)
	270	65		471
	271	22		130
	272	61		297
10	273	23		107
	274	25		399
	275	16		103
	276	16		413
	277	10		53
15	278	53		289
	279	<10		<30
	280	<10		370
	281	>100(49)		268
	282	34		48
20	283	<10		121
	284	<10		269
	285	<10		85
	286	<10		54
	287	13		228
25	288	<10		162
	289	<10		328
	290	47		281
	291	26		124
	292	14		262
30	293	<10		145
	294	15		109
	295	>100 (45)		178
	296	61		109
	297	<<10		41
35	298	<10		119
	299	<<10		53
	300	<10		-(43)
	301	43		-(39)
	302	12		202
40	303	11		188
	304	63		401
	305	11		221
	306	11		72
	307	>100(49)		165
45	308	20		101
	309	10		285
	310	67		607
	311	<10		329
	312	<<10		29
50	313	<10		330
	314	44		32
	315	<10		82
	316	10		-(40)

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	317	<<10		136
	318	10		418
	319	<<10		98
	320	<10		596
	321	<<10		37
10	322	<10		60
	323	<<10		<30
	324	12		64
	325	<10		46
	326	>100(31)		-(18)
15	327	> 100 (30)		-(6)
	328	>100 (22)		-(10)
	329	<10		253
	330	12		467
	331	<10		377
20	332	<<10		259
	333	12		712
	334	<10		484
	335	<<10		<30
	336	14		109
25	337	<10		198
	338	25		956
	339	38		197
	340	<10		107
	341	32		519
30	342	<<10		<30
	343	<10		232
	344	<10		<30
	345	30		123
	346	41		-(37)
35	347	77		228
	348	<10		90
	349	12		309
	350	<10		238
	351	<10		64
40	352	<10		195
	353	<10		80
	354	15		384
	355	24		252
	356	<10		66
45	357	<10		116
	358	<10		366
	359	28		274
	360	16		189
	361	<10		278
50	362	42		-(26)
	363	<10		72
	364	29		98
	365	<10		47

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	366	27		66
	367	55		207
	368	64		426
	369	>100		-(36)
	370	74		585
10	371	<10		541
	372			-(14)
	373	43		71
	374	<10		<30
	375	74		144
15	376	<10		41
	377	21		151
	378	14		92
	379	11		624
	380	<10		45
20	381	66		
	382	<10		28
	383	74		90
	384	>100(37)		
	385	<10		87
25	386	20		105
	387	<10		31
	388	12		60
	389	51		
	390	33		400
30	391	13		129
	392	>100(38)		432
	393	82		90
	394	<10		133
	395	19		226
35	396	19		86
	397	<10		77
	398	33		462
	399	63		327
	400	<10		671
40	401	<10		586
	403	14		93
	404	<10		81
	405	46		126
	406	<10		<30
45	407	26		68
	408	<10		192
	409	26		392
	410	12		79
	411	17		43
50	412	81		122
	413	39		50
	414	>100(27)		
	415	24		98

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	416	>100(49)		
	417	>100(42)		
	418	26		401
	419	>100(47)		
	420	16		77
10	421	<10		34
	422	<10		119
	423	<10		102
	424	47		224
	425	>100(5)		464
15	426	22		272
	427	>100(13)		364
	428	64		158
	429	54		603
	430	76		182
20	431	17		43
	432	13		<30
	433	11		<30
	434	20		<30
	435	33		445
25	436	>100(46)		878
	437	48		250
	438	>100(41)		414
	439	52		224
	440	47		351
30	441	70		1000
	442	>100(32)		-(28)
	443	15		627
	444	21		972
	445	>100(11)		941
35	446	>100(39)		-(40)
	447	>100(11)		553
	448	>100(39)		-(25)
	449	>100(26)		747
	450	>100(13)		-(46)
40	451	>100(25)		613
	452	>100(31)		-(37)
	453	>100(1)		
	454	>100(23)		
	455	77		
45	456	>100(21)		
	457	>100(29)		
	458	>100(18)		
	459	47		<30
	460	>100(15)		
50	461	60		
	462	52		575
	463	91		432
	464	55		201

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	465	56		1000
	466	>100(16)		
	467	>100(8)		
	468	>100(20)		
	469	>100(0)		-(28)
10	470	26		128
	471	>100(28)		237
	472	31		67
	473	>100(30)		259
	474	46		-(6)
15	475	15		-(24)
	476	<10		172
	477	59		248
	478	17		-(28)
	479	13		-(17)
20	480	10		-(22)
	481	16		-(3)
	482	24		-(5)
	483	20		<30
	484	12		75
25	485	>100(35)		
	486	>100(36)		
	487	>100(31)		
	488	98		
	489	58		637
30	490	21		261
	491	24		315
	492	20		321
	493	39		1000
	494	16		125
35	495	65		
	496	45		-(32)
	497	<10		82
	498	<10		140
	499	<10		98
40	500	14		199
	501	11		56
	502			-(23)
	503	87		-(36)
	504	46		-(42)
45	505	53		-(25)
	506	74		369
	507	44		787
	508			-(28)
	509	26		164
50	510	>100(3)		-(17)
	511	19		663
	512	29		1000
	513	>100(28)		720

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	514	>100(31)		-(29)
	515	>100(32)		-(21)
	516	50		-(27)
	517	38		-(33)
	518	>100(17)		
10	519	>100(22)		
	520	>100(43)		
	521	>100		
	522	>100		
	523	>100		
15	524	>100(21)		-(21)
	525	79		-(41)
	526	>100(46)		731
	527	65		875
	528	33		343
20	529	>100(38)		-(8)
	530	>100(45)		-(34)
	531			-(31)
	532	>100(44)		752
	533	64		623
25	534	51		-(35)
	535	32		-(27)
	536			-(7)
	537	>100(34)		-(34)
	538	>100(22)		768
30	539	>100(45)		415
	540	48		447
	541	70		794
	542	>100(45)		442
	543	54		328
35	544	<10		216
	545	70		254
	546	54		-(44)
	547	>100(33)		-(41)
	548	46		268
40	549	62		681
	550	77		536
	551	>100(19)		1000
	552	>100(10)		-(28)
	553	>100(40)		320
45	554	>100(14)		
	555	>100(29)		-(39)
	556	>100(13)		-(28)
	557	>100(33)		634
	558	73		724
50	559	36		711
	560	12		107
	561	<10		54
	562	80		-(27)

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	563	54		406
	564	39		291
	565	46		170
	566	17		276
	567	21		118
10	568	>100(28)		-(31)
	569	12		168
	570	23		173
	571	32		556
	572	64		262
15	573	39		348
	574	45		147
	575	27		664
	576	36		151
	577	14		328
20	578	18		104
	579	22		145
	580	14		84
	581	14		180
	582	>100(20)		-(29)
25	583	>100(17)		-(18)
	584	>100(13)		-(13)
	585	>100(32)		1000
	586	63		734
	587	67		-(16)
30	588	36		1000
	589	28		487
	590	54		296
	591	33		117
	592	23		472
35	593	51		1000
	594	>100(39)		-(10)
	595	46		-(0)
	596	63		719
	597	>100(27)		-(8)
40	598	19		423
	600	<10		208
	602	11		180
	603	>100(42)		864
	604	73		322
45	605	31		394
	606	18		263
	607	29		554
	608	<10		201
	609		45	
50	610		380	
	611		95	1073
	612		10	173
	613		56	-(29)

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	614	<10		434
	615	17		125
	616	36		224
	617	<10		172
	618	<10		948
10	619	>100(49)		-(44)
	620	<10		519
	621	30		-(30)
	622	11		355
	623	90		632
15	624	34		436
	625	>100(31)		596
	626	49		339
	627	65		774
	628	<10		81
20	629	<10		481
	630	36		-(23)
	631	39		186
	632	36		223
	633	58		-(28)
25	634	>100(40)		-(13)
	635	>100(25)		-(23)
	636	33		106
	637	52		375
	638	>100(43)		-(16)
30	639	>100(29)		-(12)
	640	35		254
	641	28		293
	642	>100(20)		-(8)
	643	>100(40)		-(2)
35	644	>100(17)		-(14)
	645	23		-(32)
	646	11		-(0)
	647	13		712
	648	16		937
40	649	39		1000
	650	32		420
	651	40		808
	652	43		115
	653	23		581
45	654	19		698
	655	43		-(43)
	656	19		-(32)
	657	40		-(27)
	658	19		389
50	659	19		1000
	660	25		835
	661	<10		75
	662	23		296

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	663	<10		202
	664	<10		97
	665	11		122
	666	10		134
	667	<10		100
10	668	<10		144
	669	23		134
	670	15		82
	671	64		-(22)
	672	53		-(9)
15	673	15		426
	674	>100(43)		854
	675	46		442
	676	26		632
	677	47		730
20	678	<10		164
	679	<10		337
	680	35		570
	681	30		270
	682	>100(30)		-(32)
25	683	>100(40)		-(26)
	684	52		549
	685	22		-(41)
	686	38		-(19)
	687	26		-(34)
30	688	34		-(19)
	689	>100(42)		571
	690	>100(10)		-(11)
	691	>100(10)		-(18)
	692	>100(35)		>1000(20)
35	693	56		>1000(46)
	694	>100(12)		-(37)
	695	>100(10)		-(37)
	696	>100(37)		-(35)
	697	<<10		211
40	698	>100(34)		-(29)
	699	13		-(29)
	700	>100(30)		-(0)
	701	<10		459
	702	<10		495
45	703	<<10		375
	704	16		177
	705	<10		147
	706	<10		227
	707	17		209
50	708	51		348
	709	19		-(19)
	710	>100(33)		-(30)
	711	>100(34)		-(17)

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	712	83		
	713	67		89
	714	16		248
	716	11		-(19)
	717	>100(8)		
10	718	<10		-(19)
	719	14		431
	720	42		30
	721	36		-(20)
	722	<10		85
15	723	17		380
	724	<10		116
	725	<10		413
	726	37		624
	727	52		
20	728	100		
	729	30		302
	730	34		634
	731	17		259
	732	48		
25	733	29		186
	734	29		216
	735	15		1000
	736	72		
	737	<10		523
30	738	11		269
	739	<10		234
	740	23		335
	741	49		
	742	92		
35	743	10		548
	744	40		
	745	53		
	746	>100(31)		
	747	35		759
40	748	85		
	749	12		-(41)
	750	17		-(43)
	751	70		-(23)
	752	>100(37)		
45	753	>100(28)		-(9)
	754	>100(7)		
	755	>100(3)		
	757	>100(45)		
	758	>100(18)		
50	759	26		323
	760	83		-(48)
	761	>100(37)		-(44)
	762	>100		

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	763	13		-(39)
	764	14		-(19)
	765	21		937
	766	>100(45)		
	772	>100(13)		550
10	773	>100		
	774	>100(17)		
	775	>100(22)		
	776		17	386
	777	11		11
15	778		6	84
	779	<10		107
	780		6	48
	781		47	135
	782		14	365
20	783		42	451
	784		6	80
	785		19	71
	786		5	46
	787		16	37
25	788		11	122
	789		13	154
	790	<3		107
	791	3		208
	792	6		301
30	793	6		335
	794	14		192
	795	5		336
	796	15		394
	797	27		403
35	798	<10		439
	799	14		1000
	800	<10		30
	801	13		70
	802	<10		-(42)
40	803	13		-(20)
	804	37		-(20)
	805	>100(14)		-(35)
	806			-(35)
	807	>100(20)		-(20)
45	808	<10		61
	809	<10		73
	810	18		269
	811	17		-(20)
	812		12	326
50	813		23	402
	814		47	405
	815		74	180
	816		73	123

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	817		53	195
	818		43	205
	819		48	212
	820		44	187
	821		39	184
10	822		17	451
	823		11	236
	824		14	268
	825		58	333
	826		53	170
15	827		38	175
	828			
	829		-(30)	-(10)
	830		-(23)	-(10)
	831		-(50)	-(19)
20	832		-(35)	-(21)
	833		452	-(26)
	834		-(23)	-(1)
	835		161	668
	836		90	-(39)
25	837		-(10)	-(19)
	838		590	-(23)
	839		-(24)	-(30)
	840		812	-(14)
	841		28	118
30	842		18	127
	843		43	263
	844		80	450
	845		>100	453
	846		>100	-(33)
35	847		>100	-(9)
	848			943
	849		65	760
	850		65	278
	851		41	75
40	852		20	179
	853		9	102
	854		40	313
	855		39	399
	856		25	255
45	857		7	195
	858		17	102
	859		8	130
	860		11	75
	861		39	132
50	862		47	933
	863		6	31
	864		23	32
	865		12	121

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	866		7	126
	867		11	191
	868		26	70
	869		23	80
	870		17	48
10	871		16	43
	872		7	32
	873		35	69
	874		>100	151
	875		40	115
15	876		40	242
	877		43	219
	878	19		65
	879	20		48
	880	16		149
20	881	>30(29)		346
	882	23		-(36)
	883	>30(30)		521
	884	44		-(30)
	885	<3		420
25	886	>100(47)		-(27)
	887	50		-(20)
	888	12		385
	889	>100(30)		-(28)
	890	95		-(39)
30	891	7		280
	892	>100(25)		-(30)
	893	52		640
	894	>100(49)		-(23)
	895	>100(33)		-(20)
35	896	96		-(31)
	897		8	938
	898		5	637
	899		62	1000
	900		10	372
40	901		65	-(27)
	902		15	299
	903		22	-(34)
	904		4	-(46)
	905	5		-(40)
45	906		47	-(29)
	907		<10	572
	908	9		757
	909		145	-(32)
	910		72	-(38)
50	911		9	498
	912		8	497
	913		8	563
	914		<10	299

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	915	9		240
	916		42	-(16)
	917	132		546
	918		18	552
	919		73	-(11)
10	920		12	448
	921		71	-(42)
	922		12	365
	923		50	-(25)
	924		23	440
15	925	35		430
	926		18	-(31)
	927	5		623
	928		5	289
	929		94	-(21)
20	930	<10		184
	931		23	516
	932		15	208
	933		18	493
	934		55	143
25	935		59	166
	936		17	427
	937		69	819
	938		31	532
	939		15	220
30	940		31	292
	941		12	145
	942		11	335
	943		19	136
	944		8	140
35	945		25	131
	946		13	142
	947		39	375
	948		104	830
	949		51	250
40	950		17	224
	951		50	124
	952		<10	317
	953		143	-(32)
	954		4	131
45	955		12	251
	956		10	326
	957		10	136
	958		17	194
	959	<10		300
50	960		13	629
	961		32	740
	962		19	-(35)
	963		59	701

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	964	20	35	-(46)
	965		51	-(24)
	966		25	233
	967			-(15)
	968		86	-(27)
10	969		48	-(19)
	970		16	300
	971		15	523
	972		7	532
	973		30	-(0)
15	974		49	-(34)
	975		26	290
	976		14	788
	977		37	824
	978		36	-(22)
20	979		29	-(25)
	980		70	811
	981		100	-(47)
	982		96	-(18)
	983		40	-(39)
25	984		27	-(30)
	985		22	-(31)
	986		<30	264
	987		117	-(32)
	988		24	-(33)
30	989	14		425
	990	19	20	481
	991			-(20)
	992		56	766
	993		52	-(35)
35	994	27		-(47)
	995	87		-(23)
	996	53		-(27)
40	997	9		264
	998	25		591
	999	29		-(45)
	1000	3		771
	1001	<10		-(34)
45	1002	<10		-(16)
	1003	24		628
	1004	10		877
	1005	28		674
50	1006	21	29	181
	1007		>30	616
	1008		51	357
	1009			243
	1010		>30	78
55	1011		44	-(20)
	1012		58	-(24)

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	1013		61	-(22)
	1014		62	-(30)
	1015		62	195
	1016	48		
	1017	48		
10	1018	10		320
	1019	22		187
	1020		35	-(11)
	1021		53	-(38)
	1022	28		202
15	1023	22		116
	1024	11		141
	1025	15		194
	1026		44	652
	1027		36	161
20	1028	<<10		545
	1029	5		126
	1030	14		337
	1031	10		254
	1032	<10		321
25	1033		67	177
	1034		27	378
	1035		>30	-(17)
	1036		57	-(29)
	1037		59	558
30	1038		80	597
	1039		26	556
	1040	<<10		414
	1041	12		98
	1042	39		107
35	1043	27		449
	1044	<10		136
	1045	17		193
	1046	38		202
	1047		>100	-(7)
40	1048	<10		250
	1049	44		
	1050	23		579
	1051	14		418
	1052	21		408
45	1053	30		178
	1054	27		-(19)
	1055	16		312
	1056		34	932
	1057		24	447
50	1058	8		-(21)
	1059		>100	550
	1060	39		-(30)
	1061		20	136

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	1062	19	15	233
	1063		27	491
	1064		12	279
	1065			566
	1066		32	279
10	1067		70	449
	1068		14	124
	1069		13	189
	1070			391
	1071		>100(17)	-(0)
15	1072	<10	-(34)	-(18)
	1073		-(23)	-(20)
	1074			289
	1075		-(17)	-(31)
	1076		204	-(7)
20	1077	48		379
	1078		371	-(32)
	1079		196	-(25)
	1080		775	-(0)
	1081		-(50)	-(47)
25	1082		573	-(15)
	1083		382	-(30)
	1084		306	-(30)
	1085		165	-(25)
	1086		-(48)	-(19)
30	1087		566	495
	1088		265	-(23)
	1089		264	-(28)
	1090		562	-(30)
	1091		605	-(39)
35	1092		-(15)	-(10)
	1093		621	-(32)
	1094		746	-(18)
	1095		-(20)	-(25)
	1096		-(30)	-(3)
40	1097		687	-(8)
	1098		70	-(41)
	1099		18	552
	1100		553	-(18)
	1101		>100(37)	-(26)
45	1102		>100(38)	-(11)
	1103		>100(25)	-(3)
	1104		77	-(23)
	1105		>100(31)	-(1)
	1106		>100(30)	-(0)
50	1107		>100 (46)	-(24)
	1108		135	962
	1109		12	353
	1110		16	113

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	1111		46	405
	1112		124	-(19)
	1113		785	785
	1114		118	674
	1115		241	-(10)
10	1116		156	878
	1117		185	-(31)
	1118		106	-(0)
	1119		334	-(27)
	1120		207	778
15	1121		7	<30
	1122	>100(48)		-(26)
	1123		-(43)	961
	1124	>100(22)		
	1125	>100(22)		-(8)
20	1126	>100(70)		-(35)
	1127	>100(8)		
	1128	>100(47)		-(17)
	1129	>100(48)		
	1130	<10		547
25	1131	51		192
	1132	<10		146
	1133	<10		42
	1134			169
	1135	<10		239
30	1136	14		639
	1137	28		-(38)
	1138			
	1139	12		783
	1140	>100(22)		
35	1141	<10		416
	1142	80		
	1143	>100(32)		
	1144	28		-(30)
	1145			548
40	1146	23		552
	1147	10		105
	1148	<10		42
	1149	43		150
	1150	51		192
45	1151	<10		146
	1152	<10		1000
	1153	43		-(13)
	1154	49		-(21)
	1155	17		-(31)
50	1156	>100(35)		-(28)
	1157	<10		
	1158	46		
	1159	>100		

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(continued)

	Example No.	PDGF(E)	PDGF(D)	c-kit
5	1160	<10		
	1161	<10		
	1162	13		
	1163	>100		
	1164	<10		
10	1165	>100		
	1166	<10		
	1167	>100		
	1168	<10		
	1169	37		
15	1170	<10		
	1171	13		
	1172	34		
	1173	>100		
	1174	>100		
20	1175	37		
	1176	>100		
	1177	17		
	1178	78		
	1179	14		327
25	1180	<<10		480
	1181	35		-(26)
	1182	<10		206
	1183	<10		427
	1184	55		
30	1185	13		-(26)
	1186	<<10		405
	1187	24		1000
	1188	76		
	1189	26		73
35	1190	24		240
	1191	31		193
	1192	19		672
	1193	<10		-(18)
	1194	56		1000
40	1195	21		530
	1196	>100		700
	1197	25		219
	1198	<10		247
	1199	42		1000
45	1200	25		716
	1201	<10		450
	1202	50		-(15)
	1203	<10		1000
	1204	18		434
50	1206			-(27)
	1207			-(16)
	1208			-(22)
55				

Pharmacological Test Example 4: Rat carotid balloon injury model

[1475] Wistar male rats (330 to 370 mg) were anesthetized with pentobarbital anesthesia, the right femoral region was incised from the rats, a Fogarty 2F catheter was inserted through the right femoral artery and was led to the left carotid artery, and abrasion was made three times with an expansion diameter of 2.5 mm.

[1476] The test compound was suspended in 1% cremophore, and the suspension was orally administered at 0.4 ml/100 g B.W. twice a day through an oral probe for rats for 2 weeks from the day before an operation. On the second week after the operation, the rats were sacrificed by ether. The left carotid artery was removed and was fixed in buffered formalin. Sliced preparations embedded in paraffin were stained with HE and were subjected to image analysis for the measurement of the neointima area (I) and media area (M) in the section of injured blood vessel. I/M was calculated as an index for the evaluation of drug efficacy.

[1477] The results were as follows.

Example No	in vivo (dose: 30 mg/kg) I/M ratio, inhibition (%)
223	41
287	37
408	50
421	42
516	32
567	24*
590	86
614	92
615	43
622	38
647	32*
679	54*
687	17*

(* dose: 10 mg/kg)

Pharmacological Test Example 5: Measurement of inhibitory activity against KDR phosphorylation

[1478] NIH 3T3 cells (Sawano A et al., Cell Growth & Differentiation, 7, 213 - 221 (1996)) prepared by transfection of human KDR were cultured in a DMEM medium containing 10% FBS (GIBCO BRL) within a 5% carbon dioxide incubator until 50 to 70% confluent. The harvested cells were inoculated into wells of a collagen-type one-coat 96-well flat-bottom plate, each containing the same medium, in an amount of 1.5×10^4 per well, followed by cultivation at 37°C overnight. The medium was then replaced by a DMEM medium containing 0.1% FBS. A solution of a test compound in dimethyl sulfoxide was added to each well, and the cultivation was carried out at 37°C for additional one hr. A human recombinant vascular endothelial growth factor (hereinafter abbreviated to "VEGF") was added to a concentration of 100 ng/ml, and the stimulation of cells was carried out at 37°C for 2 min. The medium was removed, the cells were washed with phosphate buffered saline (pH 7.4), and 50 μ l of a solubilization buffer (20 mM HEPES (pH 7.4), 150 mM NaCl, 0.2% Triton X-100, 10% glycerol, 5 mM sodium orthovanadylate, 5 mM disodium ethylenediaminetetraacetate, and 2 mM $\text{Na}_4\text{P}_2\text{O}_7$) was then added thereto. The mixture was shaken at 4°C for 2 hr to prepare a cell extract.

[1479] An anti-phospho-tyrosine antibody (PY20; Transduction Laboratories) was immobilized on a microplate for ELISA (Maxisorp; NUNC), and the whole quantity of the cell extract was transferred to the wells, and the immobilized antibody was reacted with the phosphorylated protein at 4°C overnight. After washing, an anti-KDR antibody (Santa Cruz) was allowed to react at room temperature for one hr, and, further, after washing, a peroxidase-labeled anti-rabbit Ig antibody (Amersham) was allowed to react at room temperature for one hr. After washing, a chromophoric substrate for peroxidase (Sumitomo Bakelite Co., Ltd.) was added thereto and was allowed to react at room temperature. After a suitable level of color development, a reaction termination solution was added to stop the reaction, and the absorbance at 450 nm was measured with a microplate reader. The KDR phosphorylation activity for each well was determined by presuming the absorbance with the addition of VEGF and without the addition of the medicament to be 100% KDR phosphorylation activity and the absorbance without the medicament and VEGF to be 0% KDR phosphorylation activity.

[1480] The concentration of the test compound was varied on several levels, the inhibition (%) of KDR phosphorylation was determined for each case, and the concentration of the test compound necessary for inhibiting 50% of KDR

phosphorylation (IC_{50}) was calculated.

[1481] The results were as follows.

Example No.	IC_{50} (nM)
223	38
287	> 1000
408	108
421	692
516	> 1000
567	> 1000
590	> 1000
614	47
615	37
622	> 1000
647	599
679	323
687	176

Pharmacological Test Example 6: Porcine coronary balloon injury model

[1482] Edible shoats (24 to 31 kg) were anesthetized with telazol and xylazine, a balloon catheter was inserted through the femoral artery, and the descending branch in front of the heart on the left and the right rotator branch were injured under vasography.

[1483] For 28 days from the operation, the compound of Example 679 was orally administered as a gelatin capsule at a dose of 10 mg/kg twice a day. Further, only a gelatin capsule was administered as a control. In the test, each group consisted of 6 shoats.

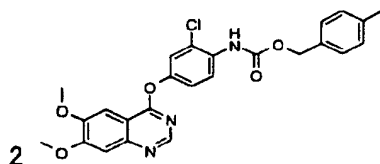
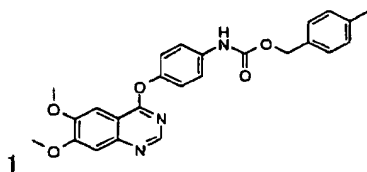
[1484] On the 28th day from the operation, the shoats were sacrificed with pentobarbital and were perfused with buffered formalin, and the heart was then removed. Paraffin embedded preparations of the injured blood vessel portion were sliced and stained with HE, followed by image analysis to measure the intima area (IA), media area (MA), and vessel area (VA), and the fissure length (FL) and vessel perimeter (VP) of the inner elastic plate.

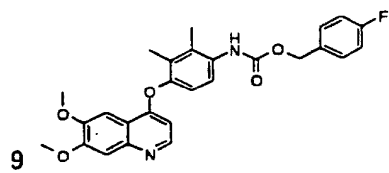
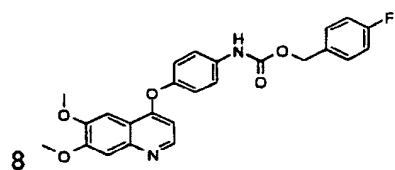
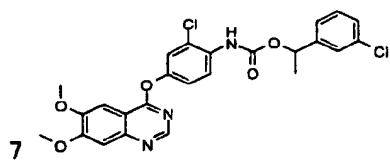
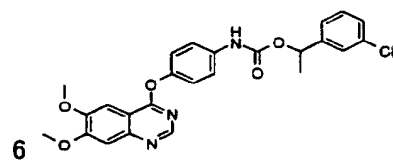
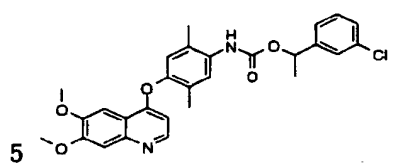
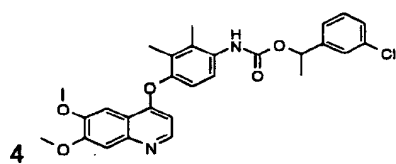
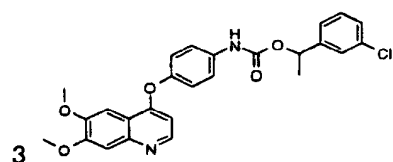
[1485] IA/MA and $(IA/VA)/(FL/VP)$ were calculated as an index for the evaluation of drug efficacy.

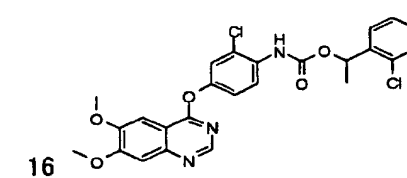
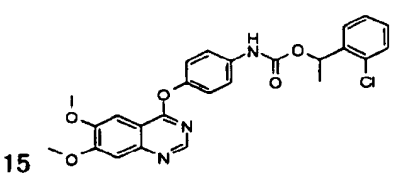
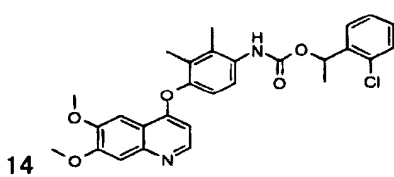
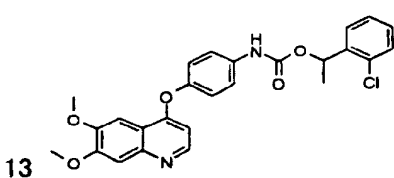
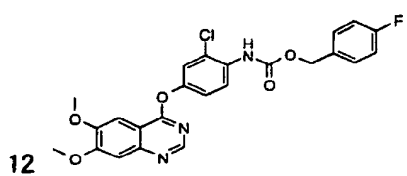
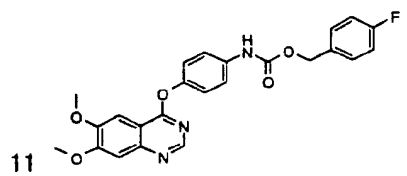
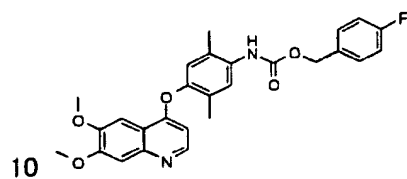
[1486] The results were as follows.

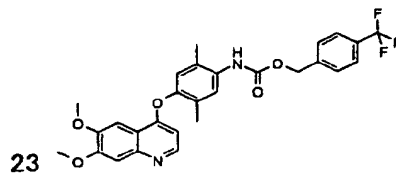
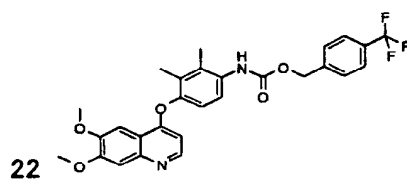
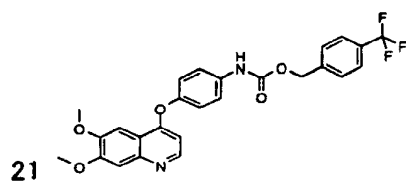
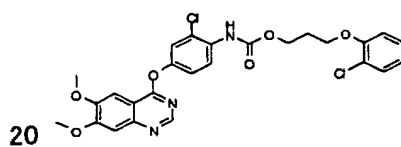
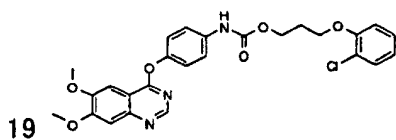
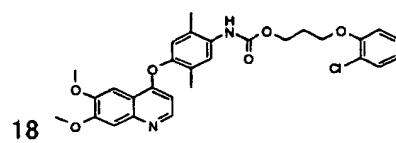
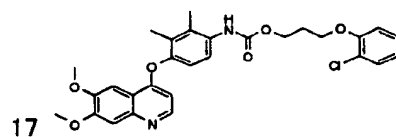
Dose (mg/kg)	IA/MA inhibition(%)	$(IA/VA)/(FL/VP)$ inhibition (%)
Control	-	-
10	36 ($p < 0.05$)	47 ($p < 0.001$)

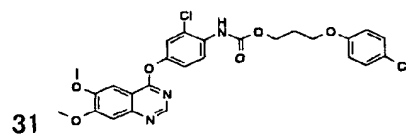
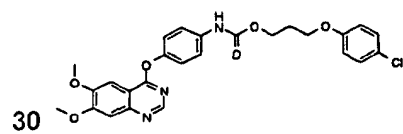
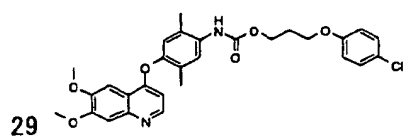
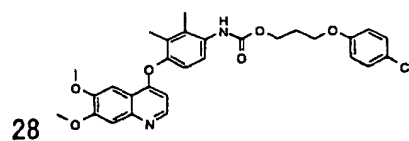
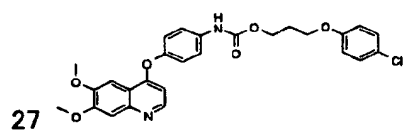
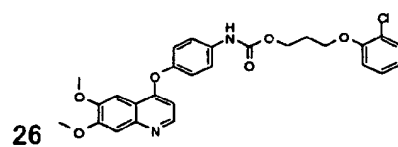
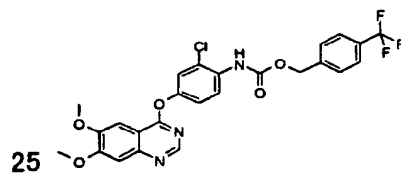
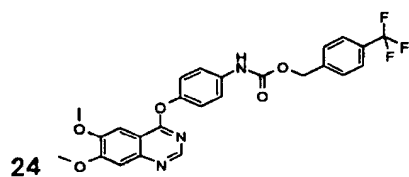
[1487] The compounds described in the examples have the following structures.

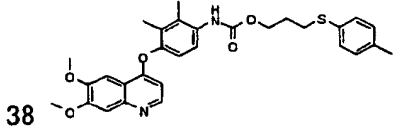
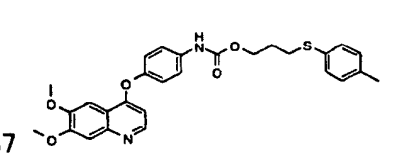
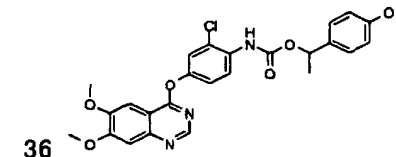
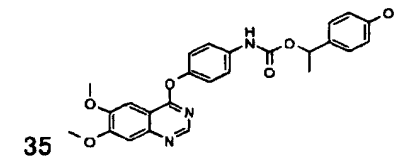
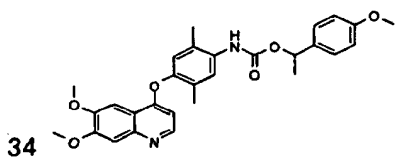
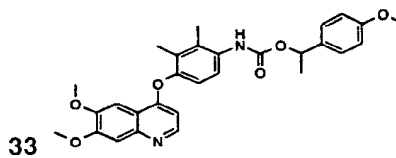
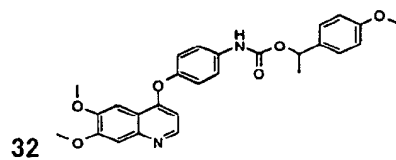


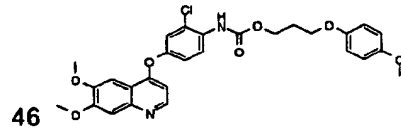
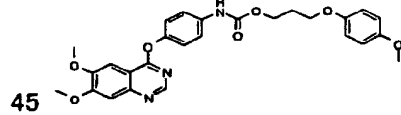
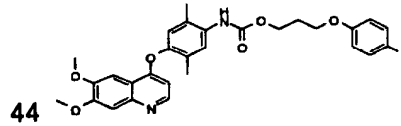
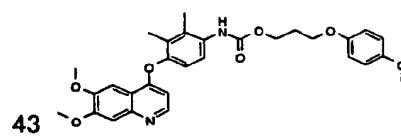
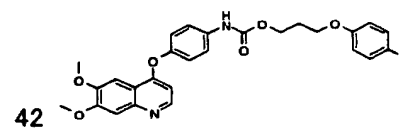
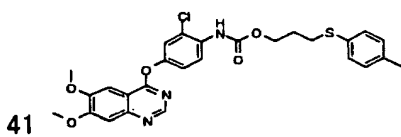
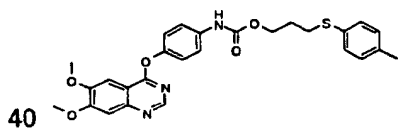
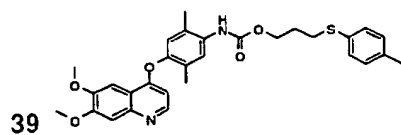


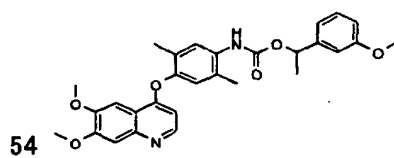
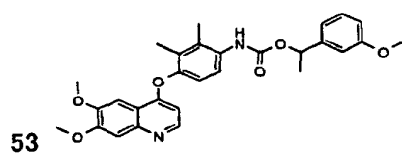
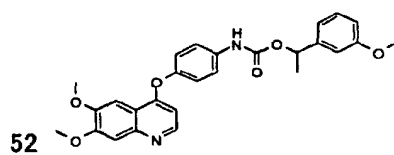
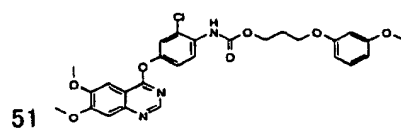
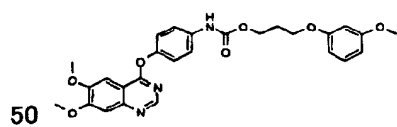
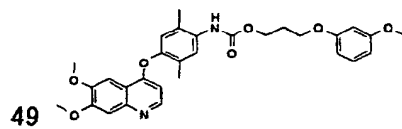
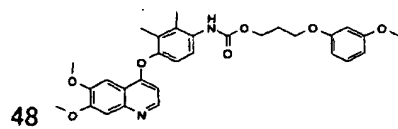
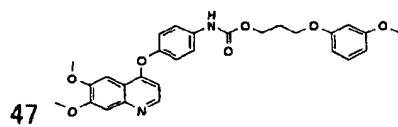


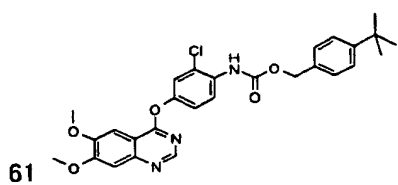
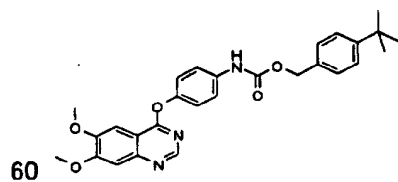
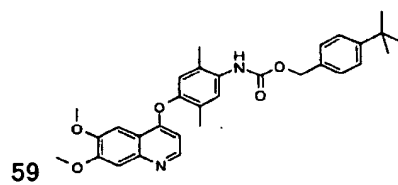
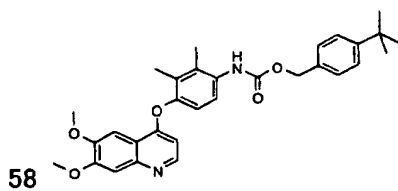
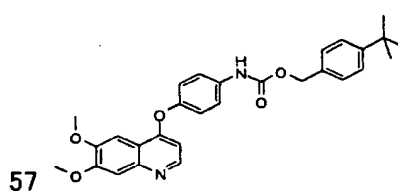
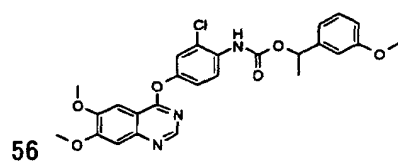
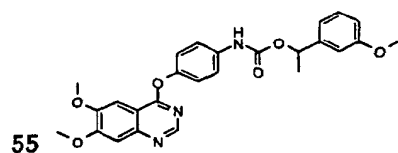




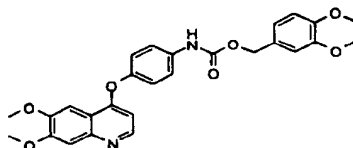




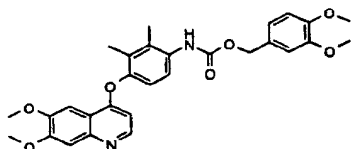




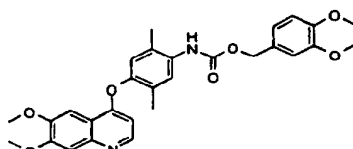
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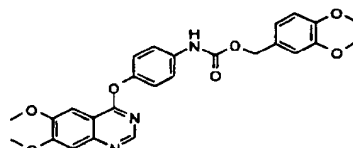
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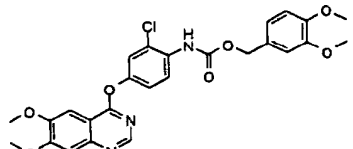
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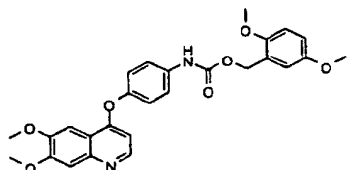
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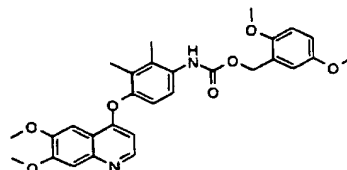
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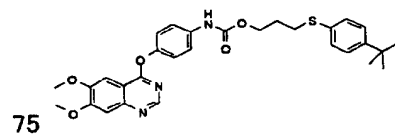
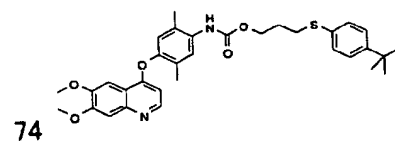
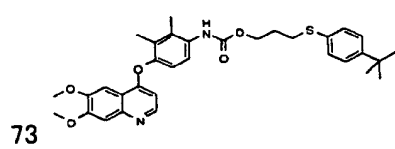
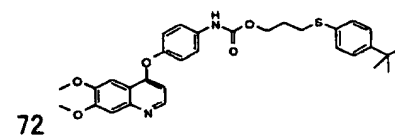
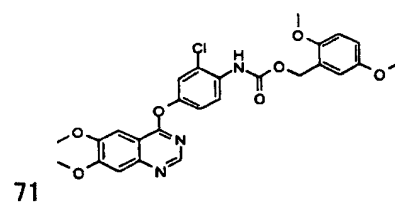
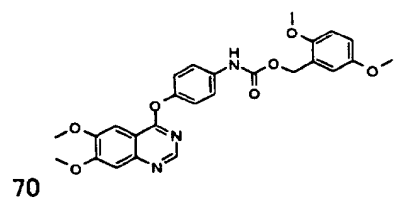
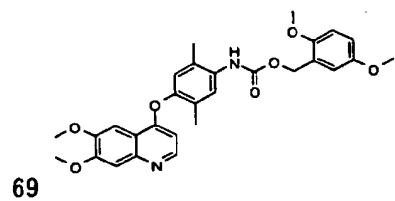


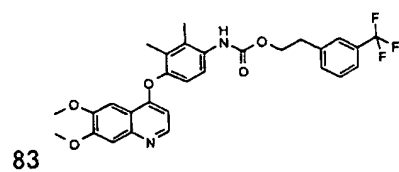
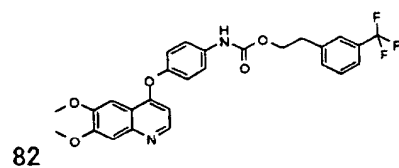
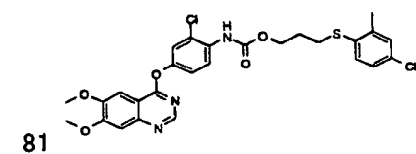
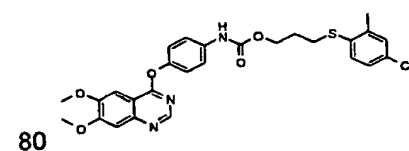
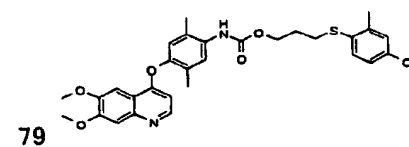
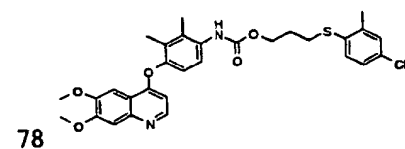
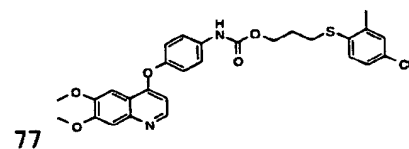
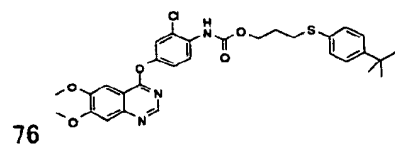
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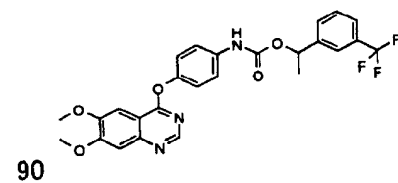
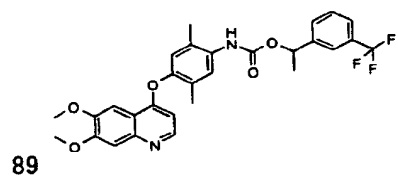
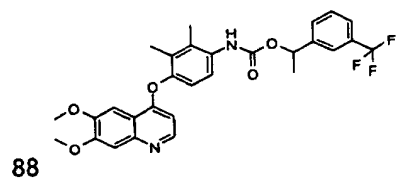
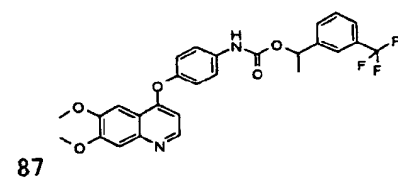
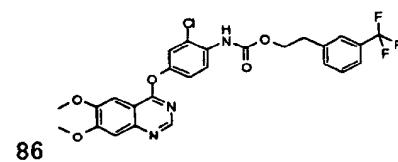
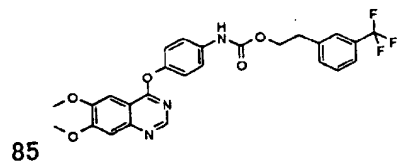
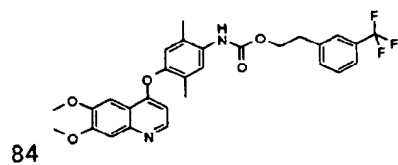


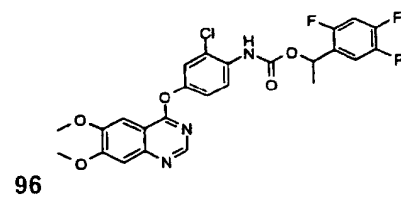
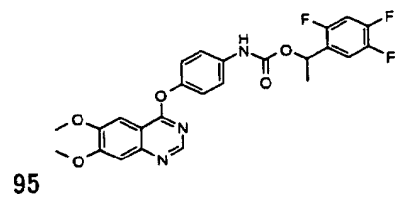
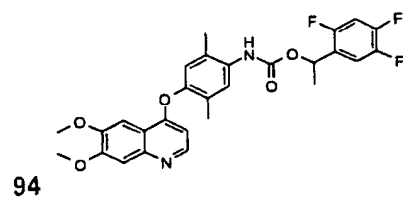
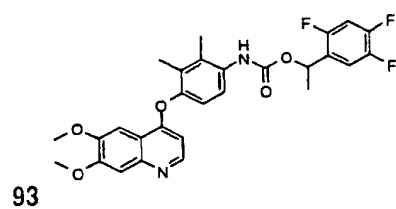
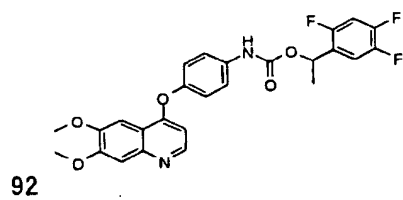
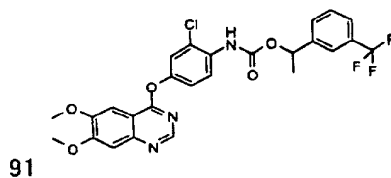
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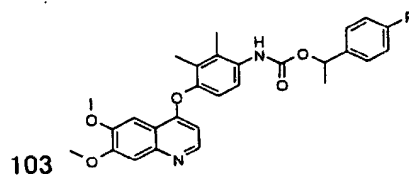
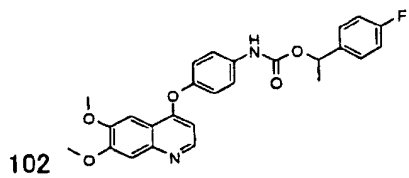
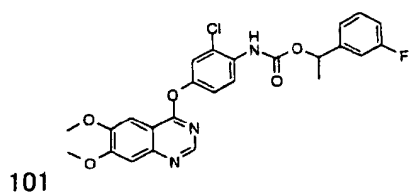
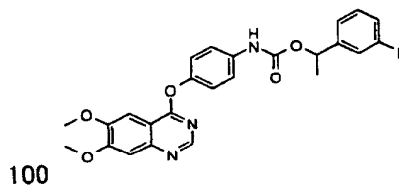
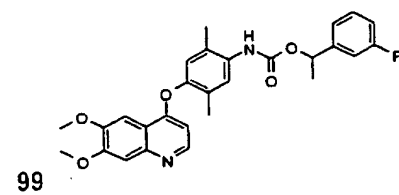
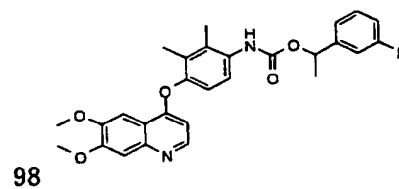
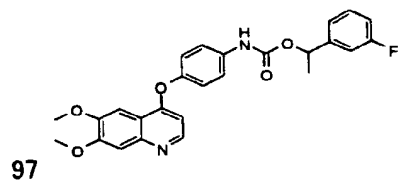


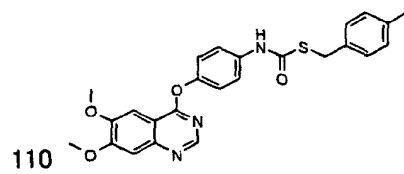
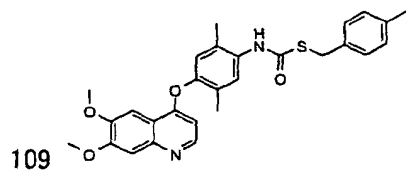
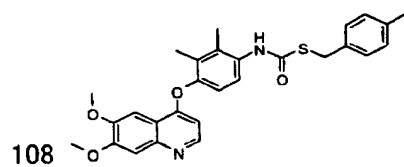
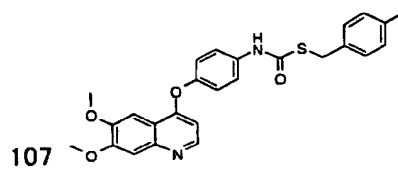
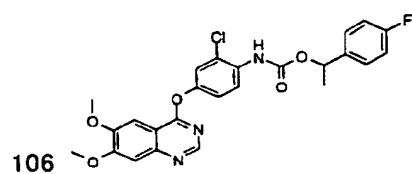
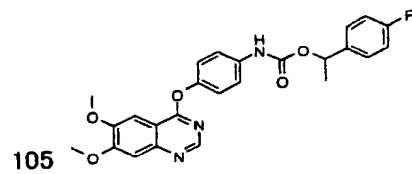
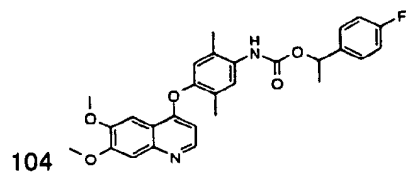




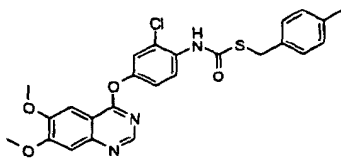




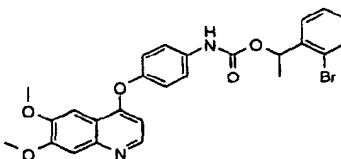




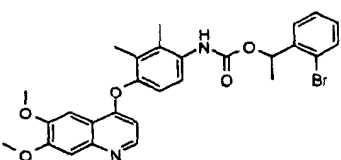
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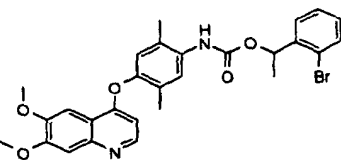
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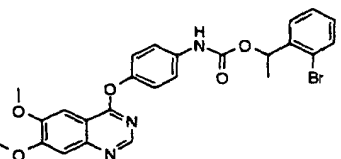
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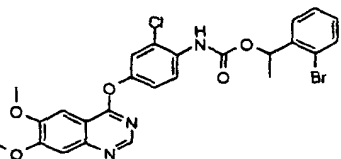
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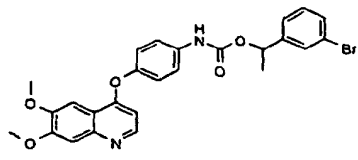
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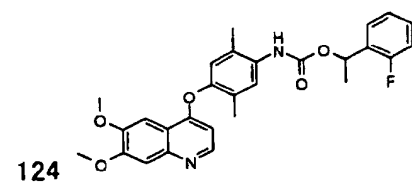
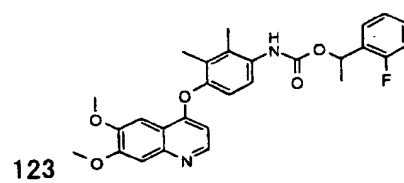
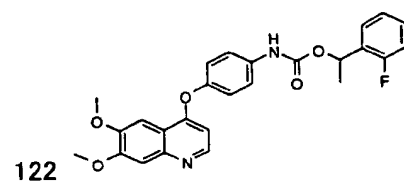
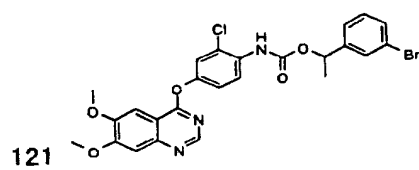
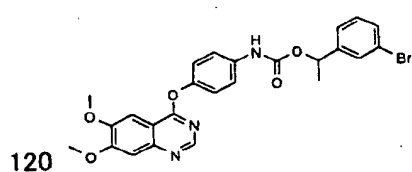
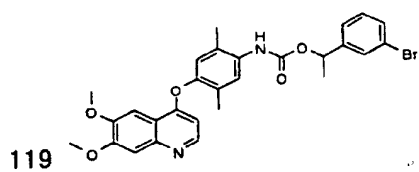
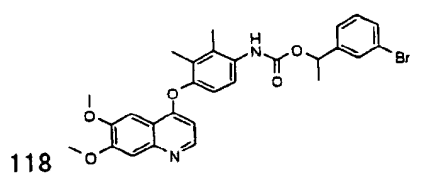


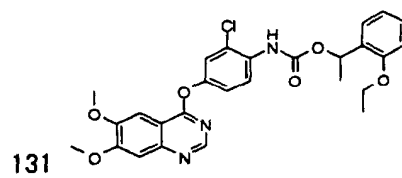
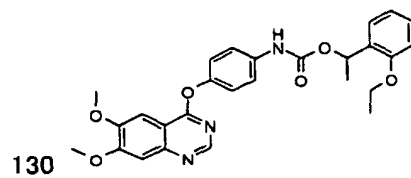
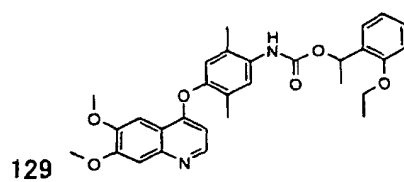
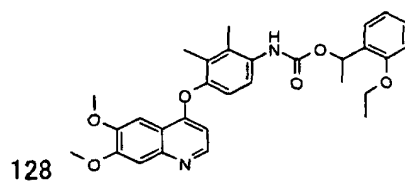
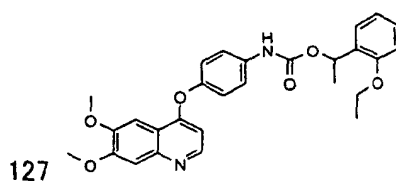
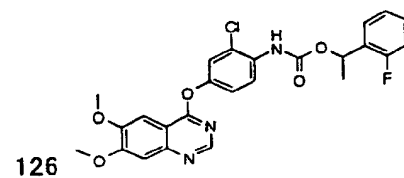
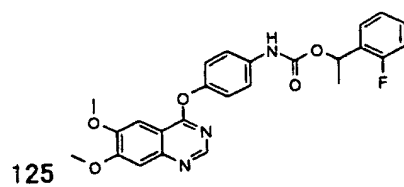
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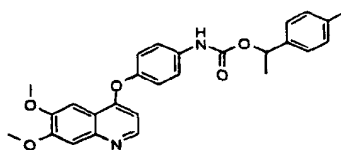
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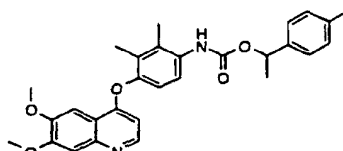




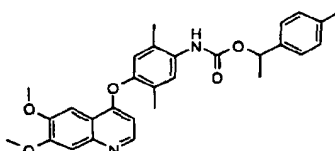
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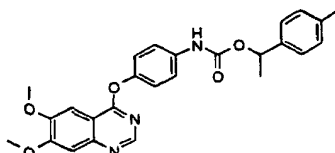
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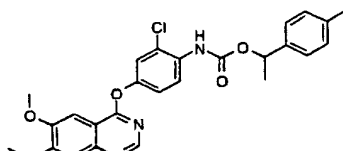
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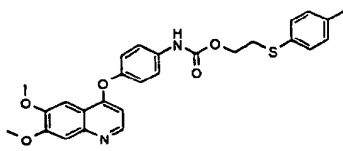
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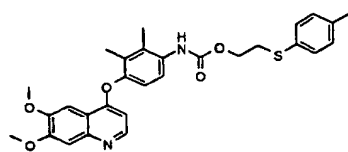
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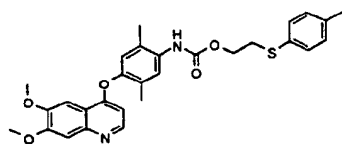
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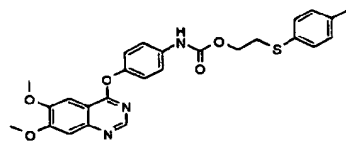
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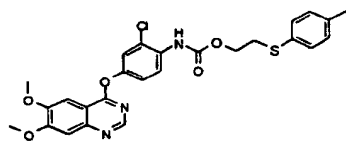
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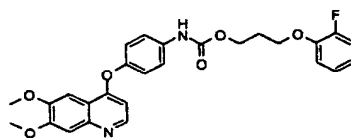
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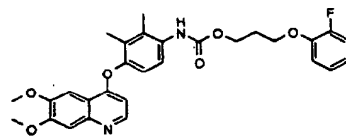
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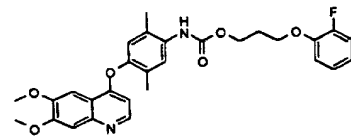
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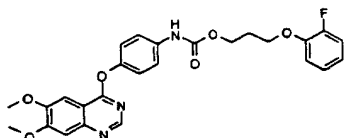
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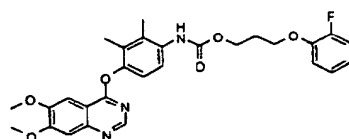
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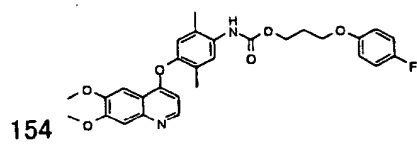
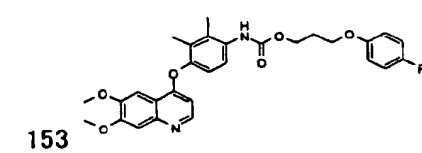
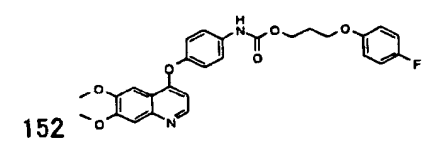
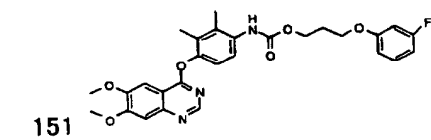
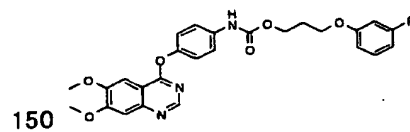
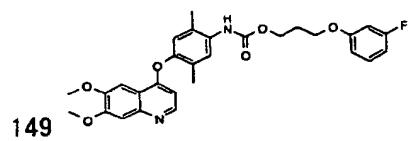
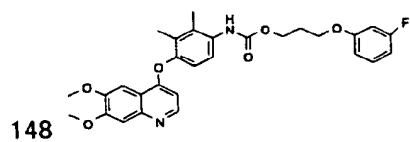
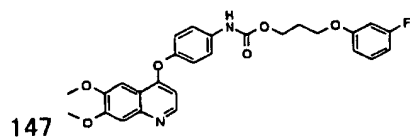


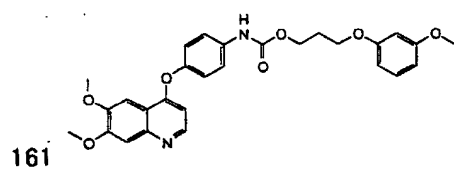
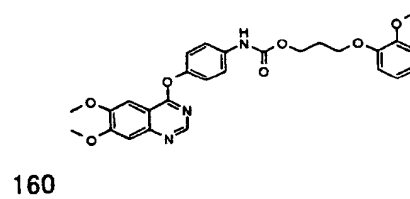
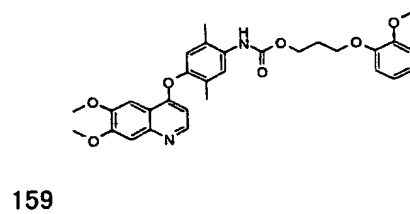
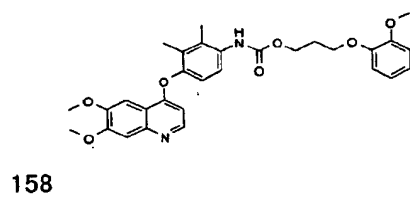
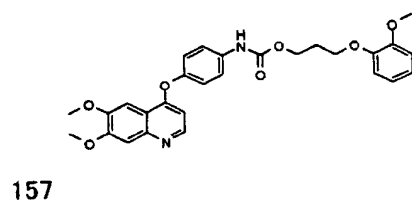
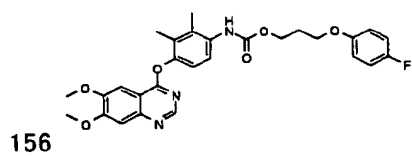
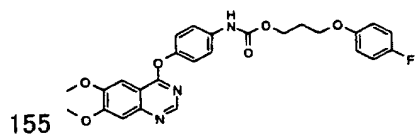
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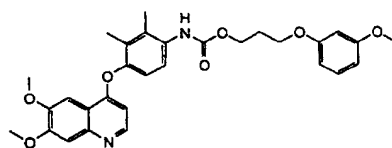
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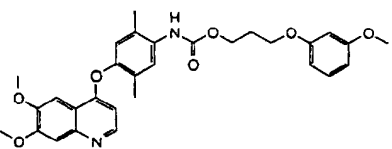




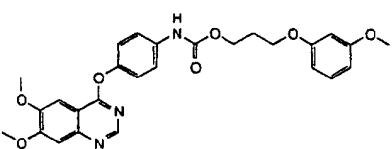
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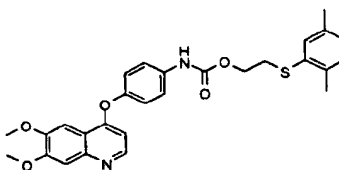
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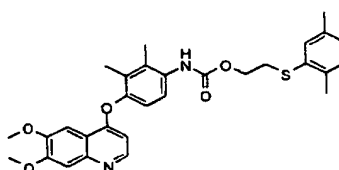
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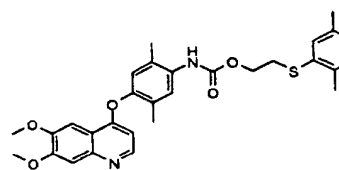
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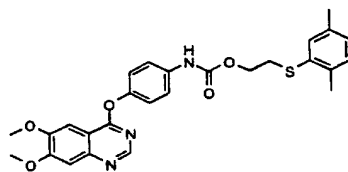


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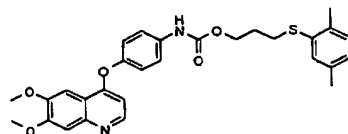


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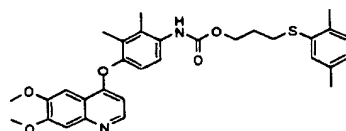




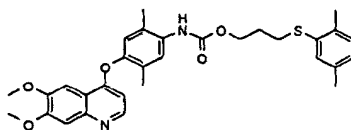
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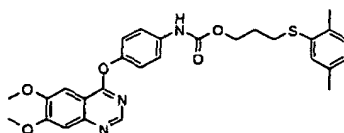
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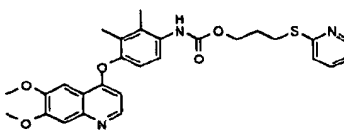
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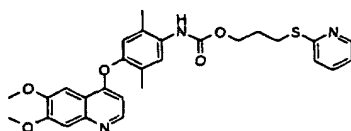
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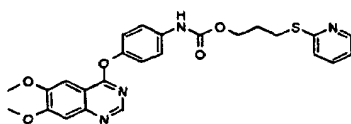
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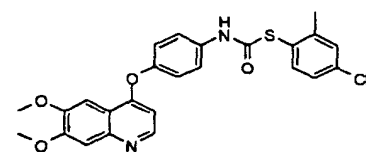
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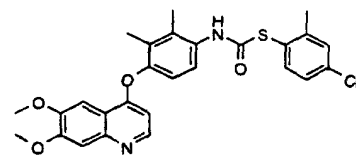
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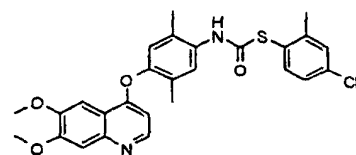
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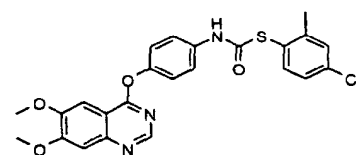
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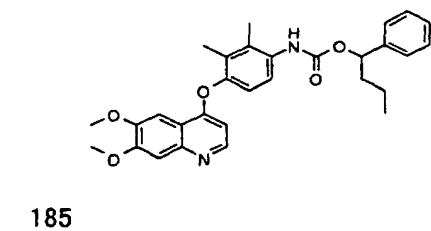
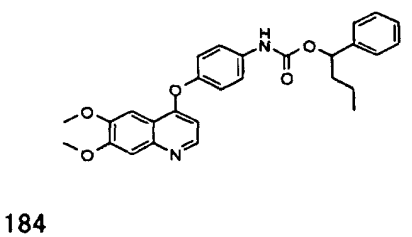
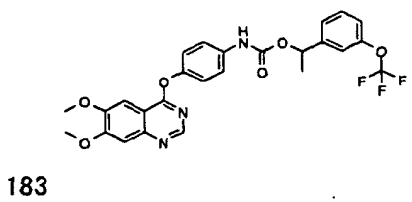
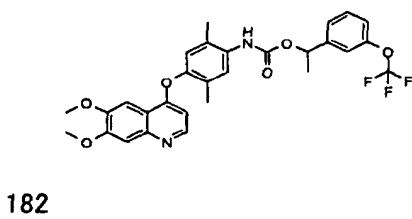
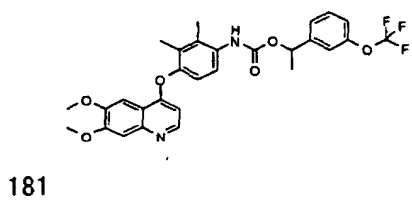
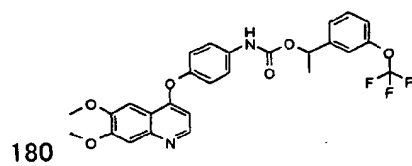
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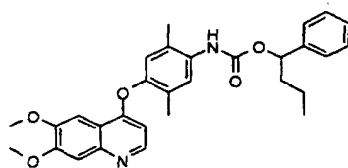
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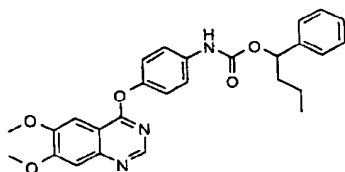
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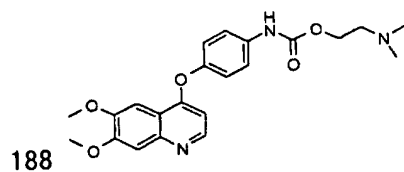
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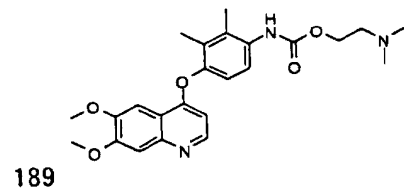
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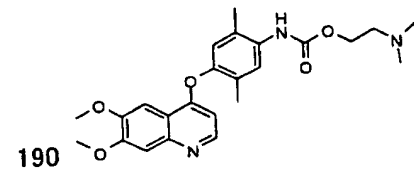
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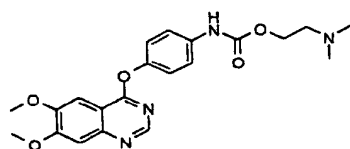


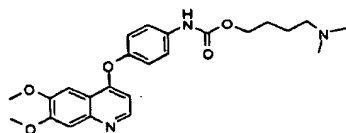
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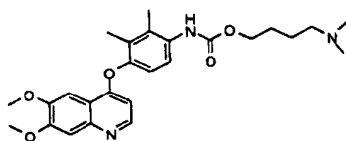
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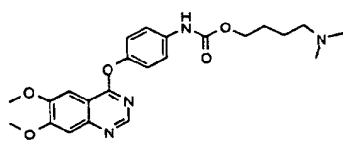




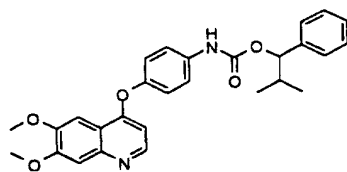
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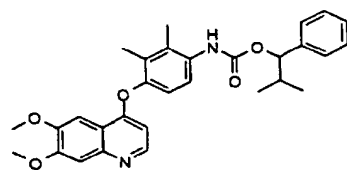
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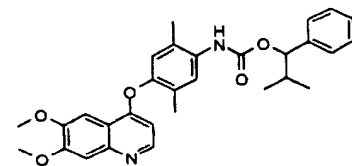
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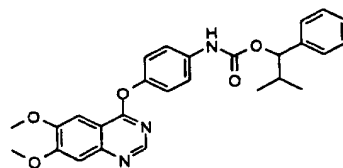
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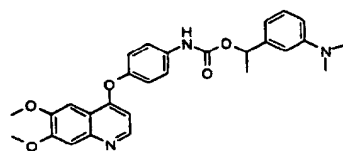
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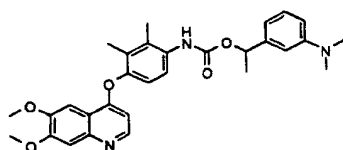
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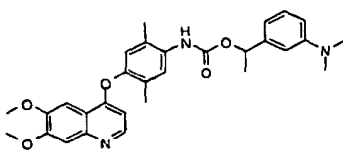
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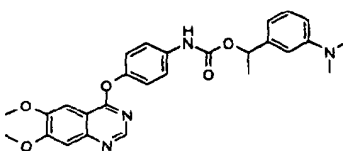
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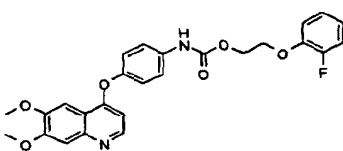
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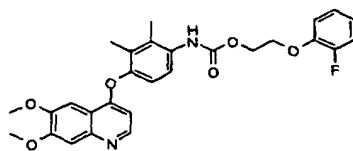


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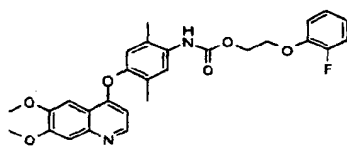
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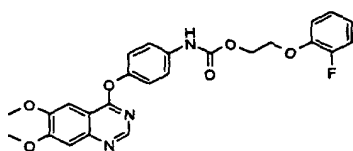
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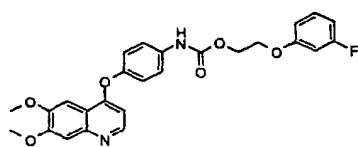
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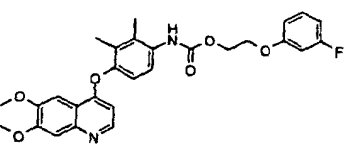
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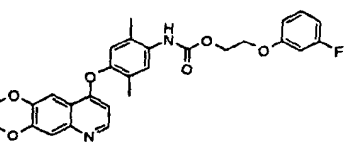
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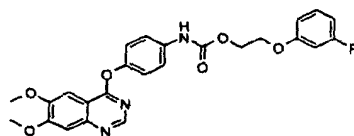
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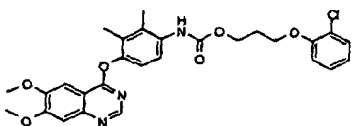


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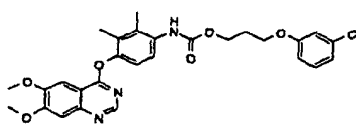
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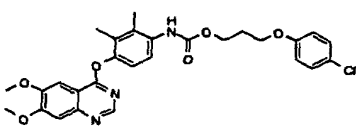
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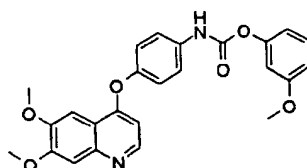
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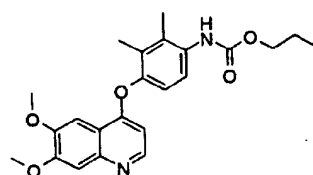
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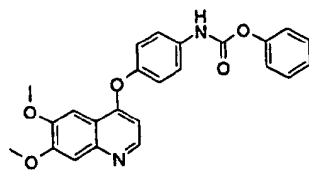


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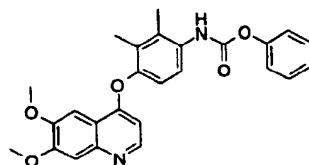


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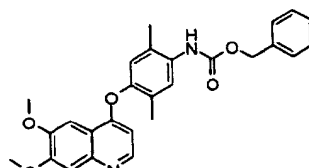
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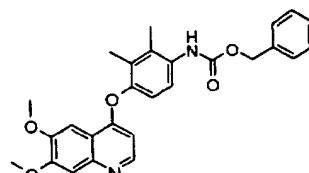
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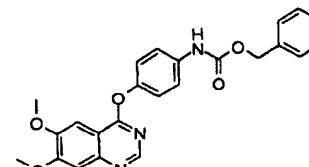
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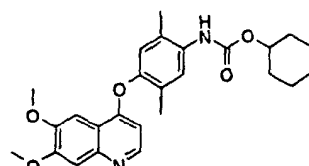
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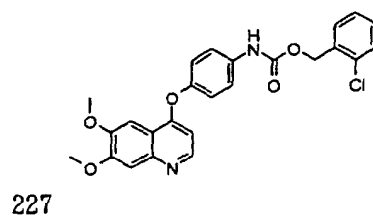
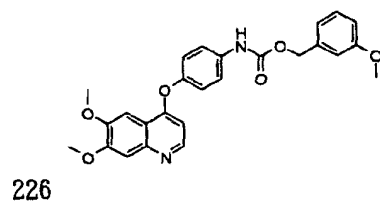
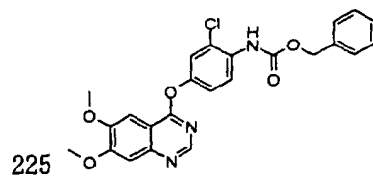
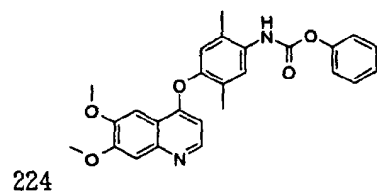
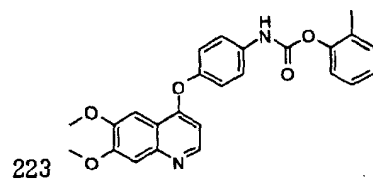
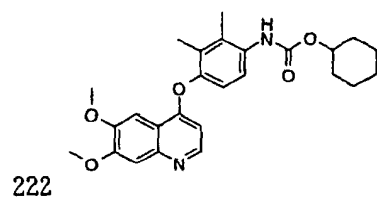


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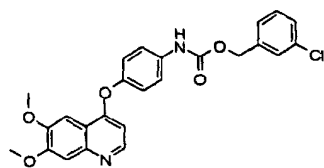


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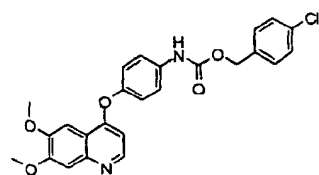


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228

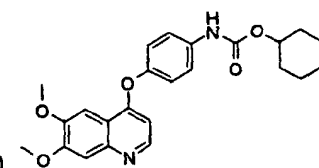
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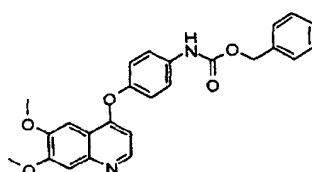
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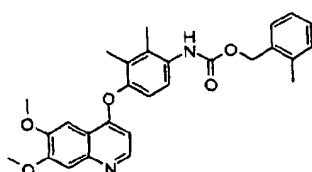
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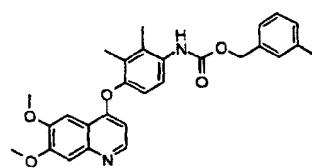
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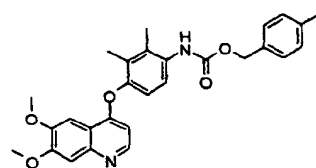


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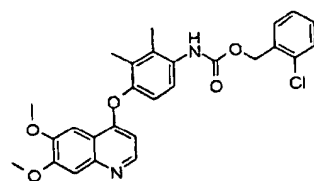
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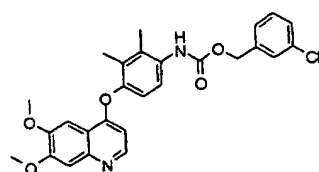
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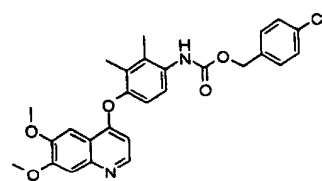
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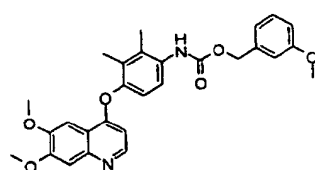
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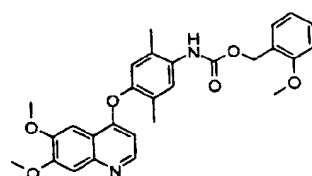
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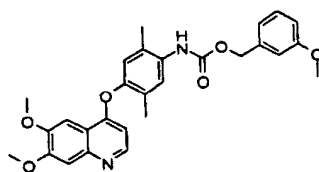
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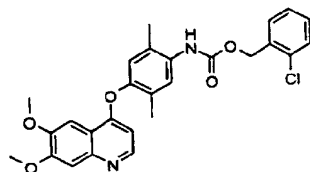
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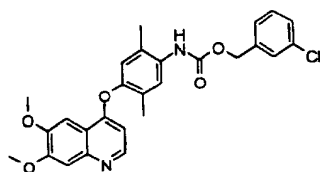
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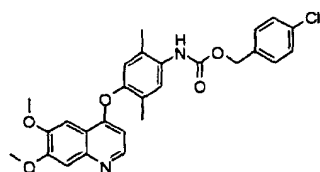
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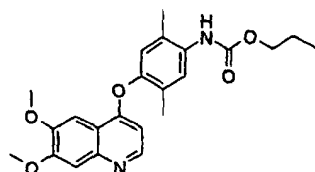
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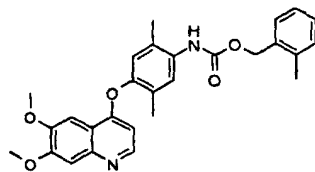
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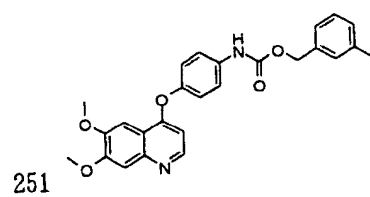
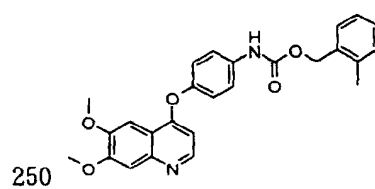
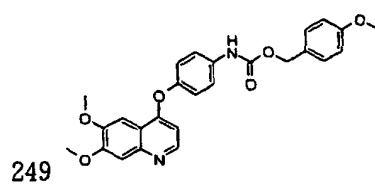
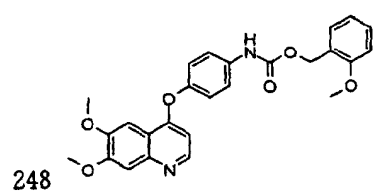
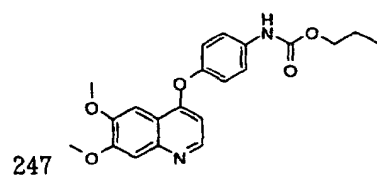
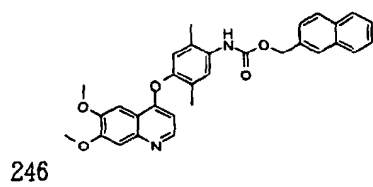
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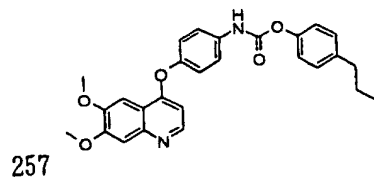
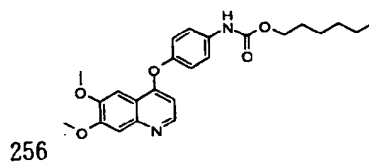
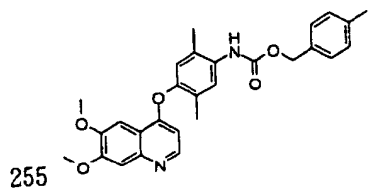
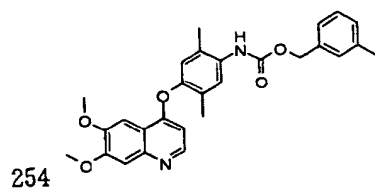
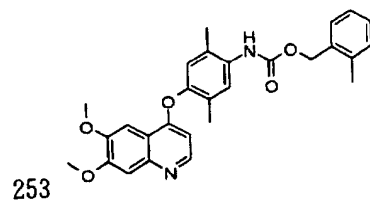
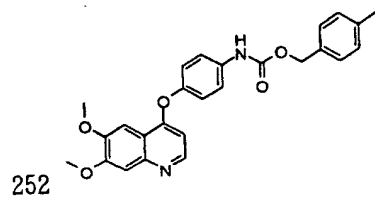
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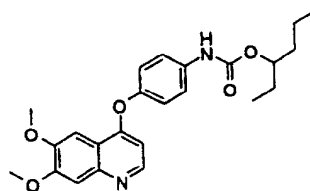


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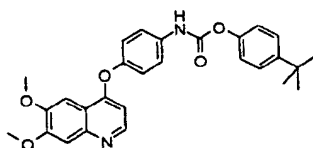
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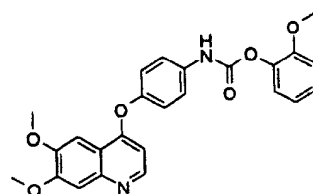
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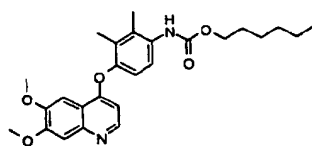
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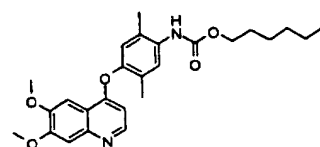
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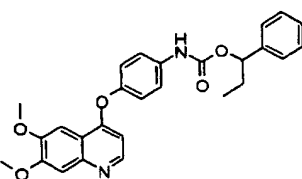
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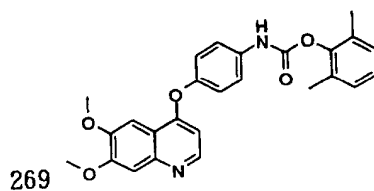
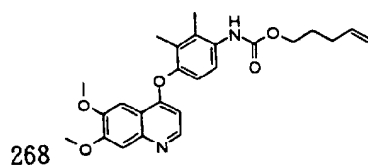
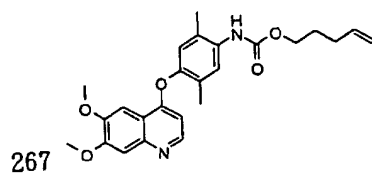
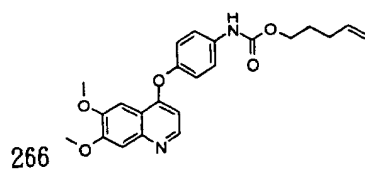
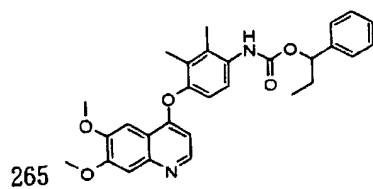
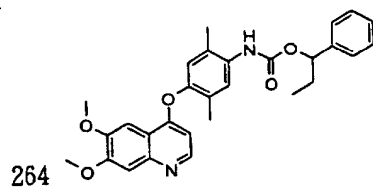
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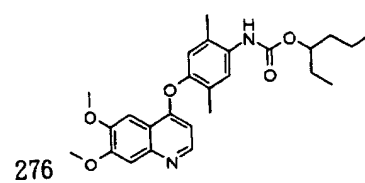
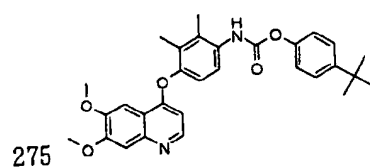
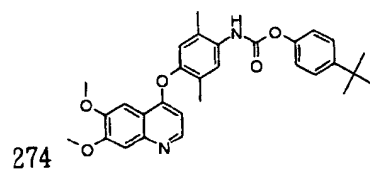
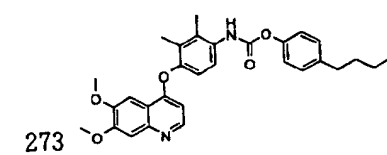
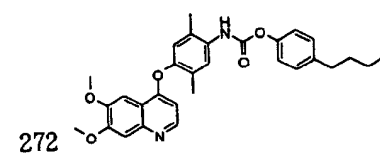
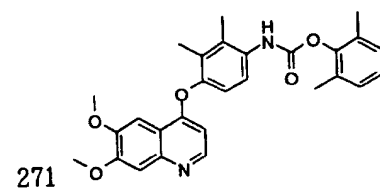
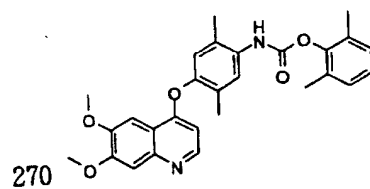
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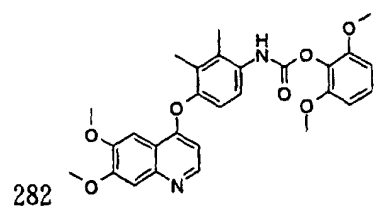
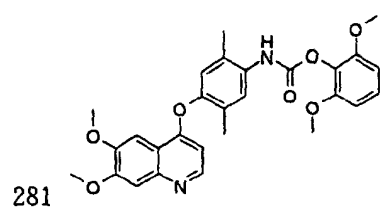
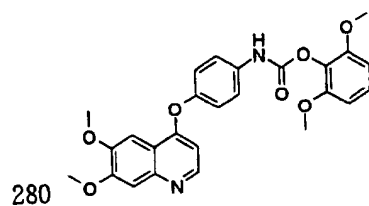
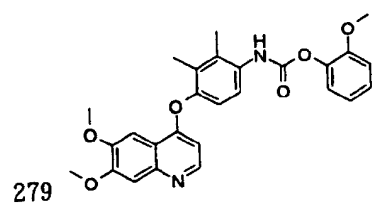
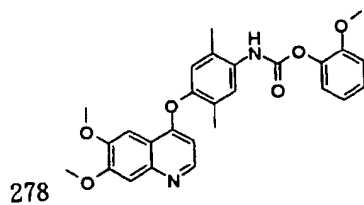
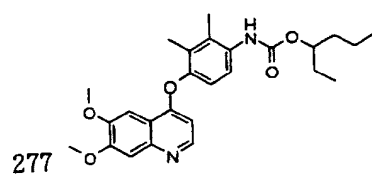


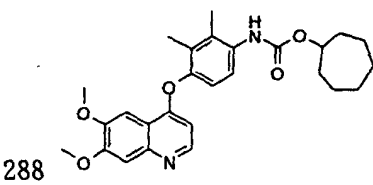
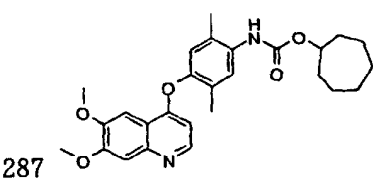
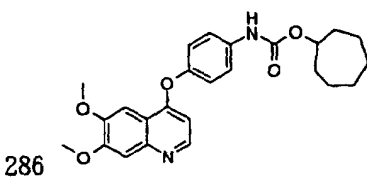
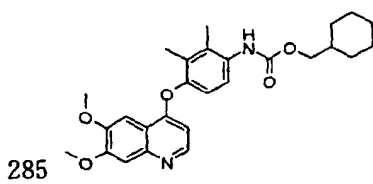
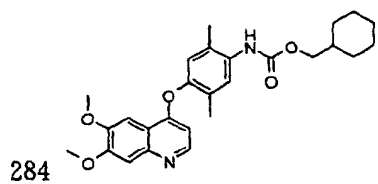
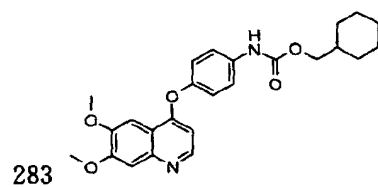
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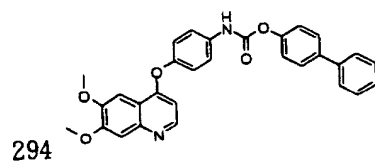
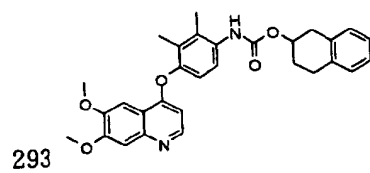
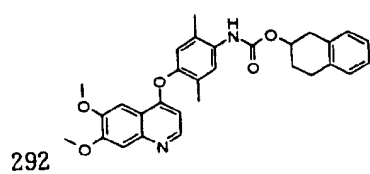
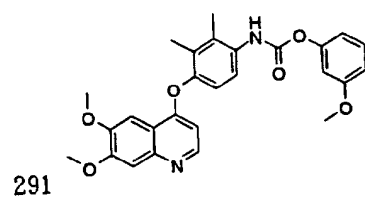
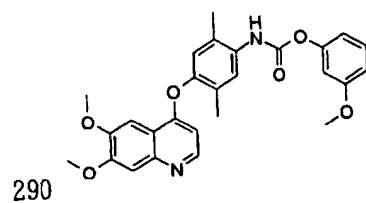
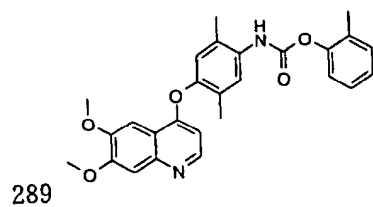
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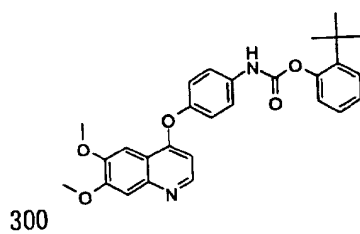
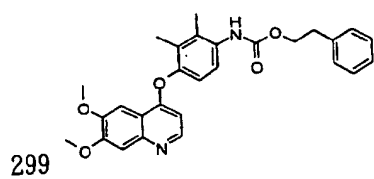
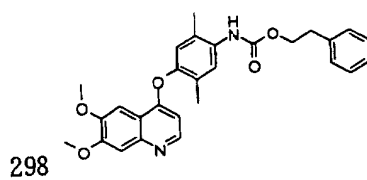
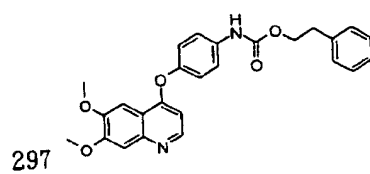
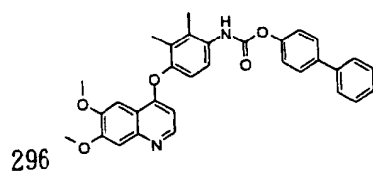
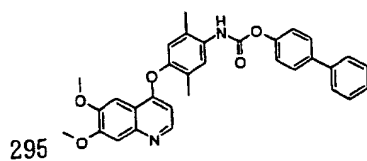


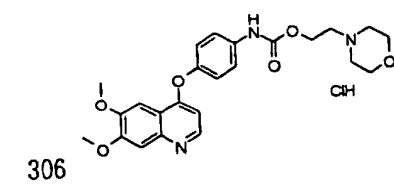
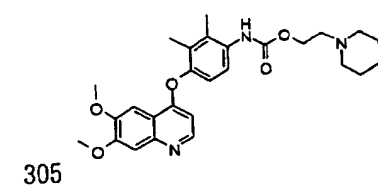
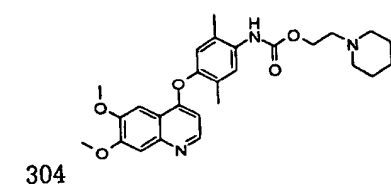
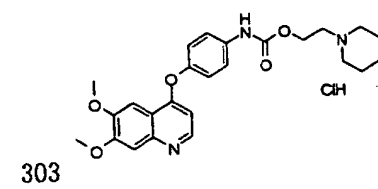
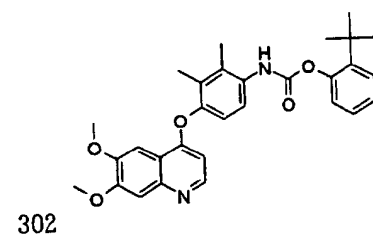
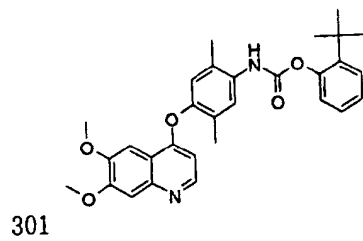




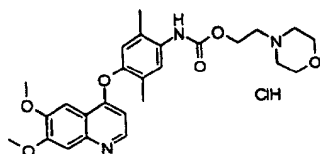




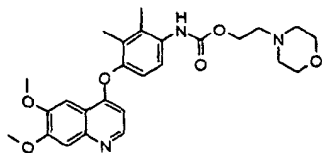




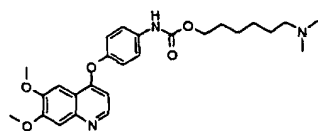
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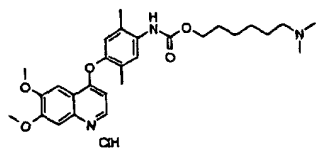
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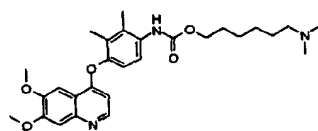
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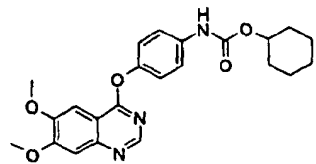
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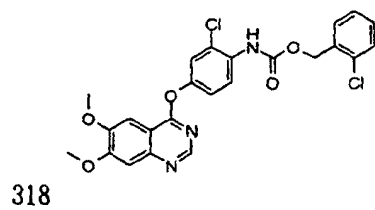
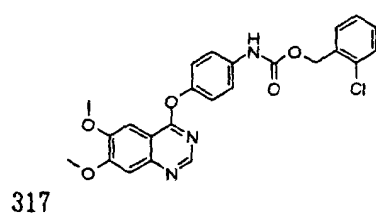
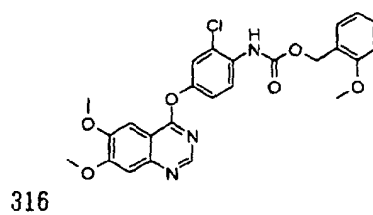
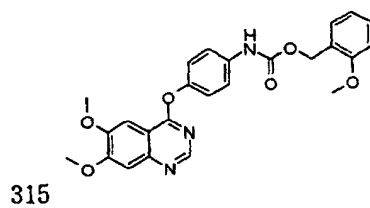
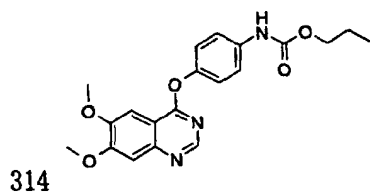
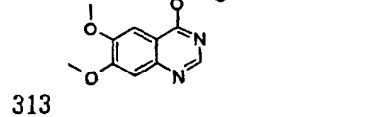


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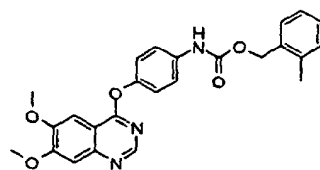
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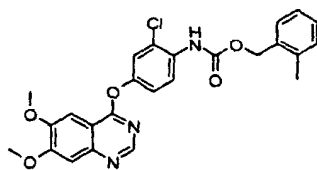
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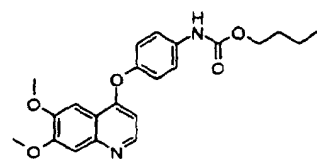
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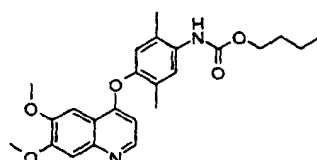
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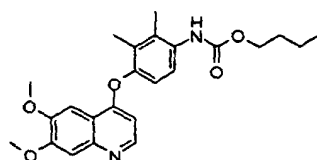
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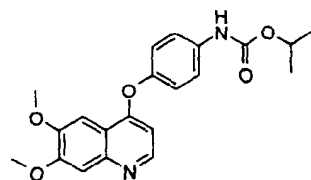
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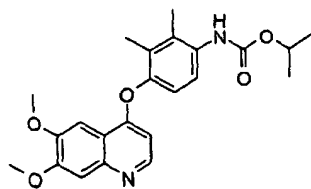
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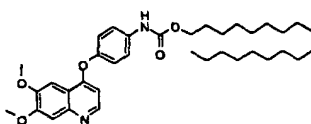
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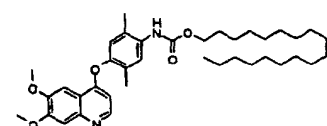
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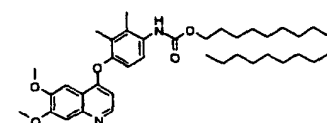
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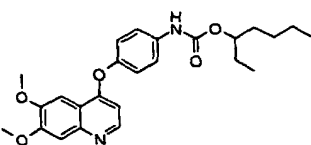
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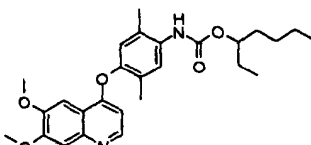
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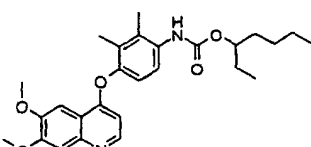
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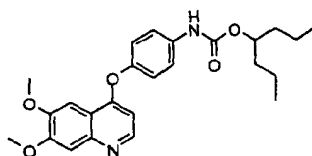
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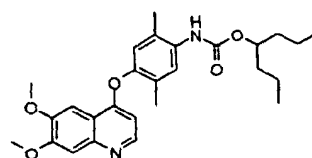
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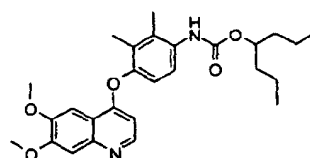
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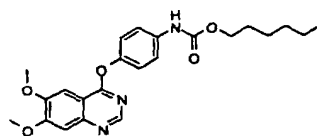
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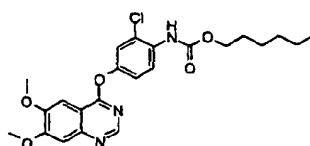
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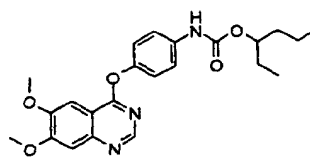
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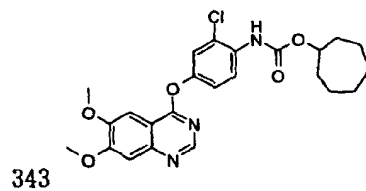
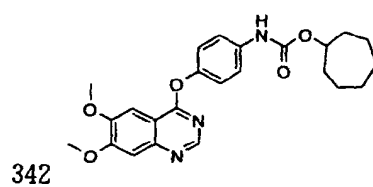
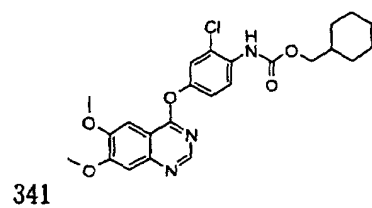
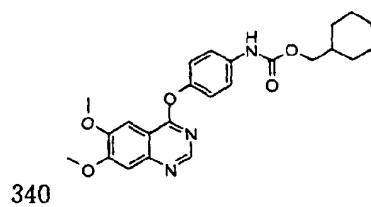
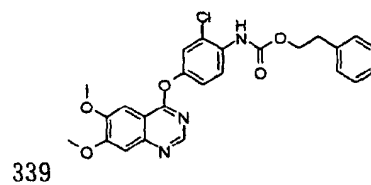
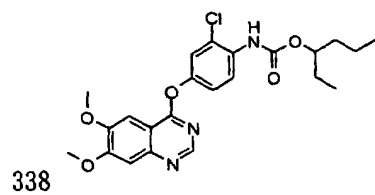


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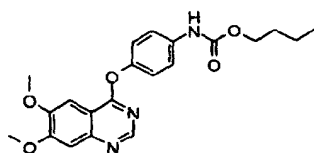


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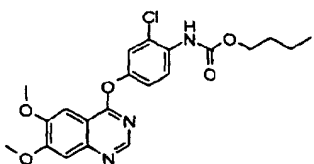




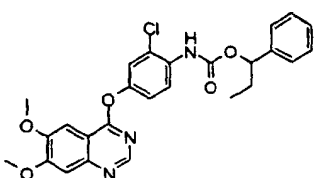
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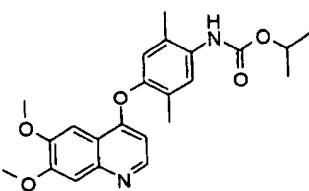
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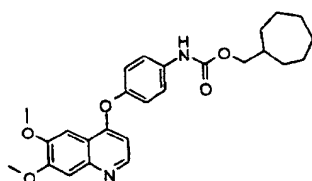
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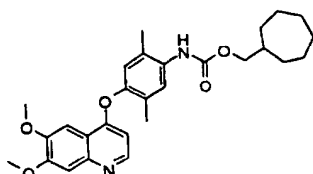
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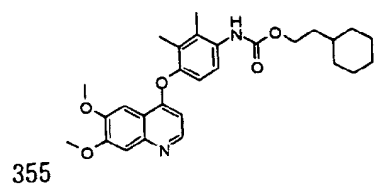
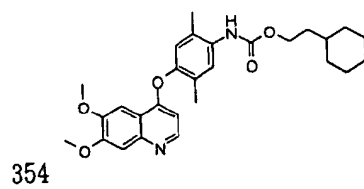
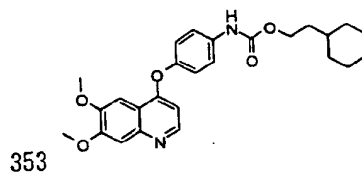
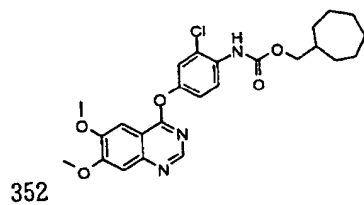
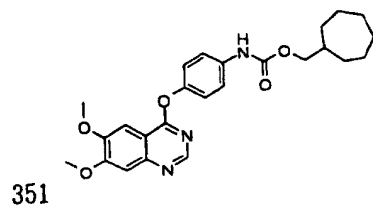
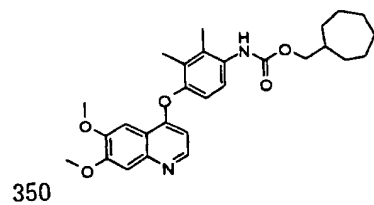


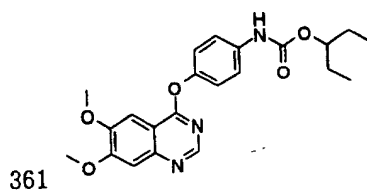
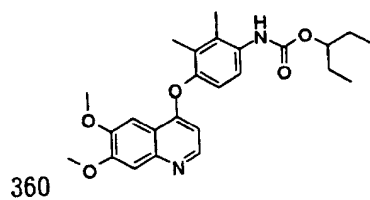
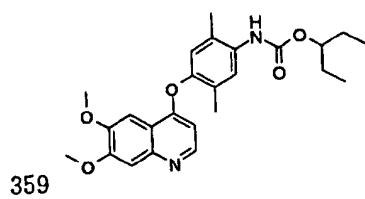
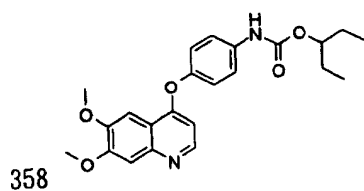
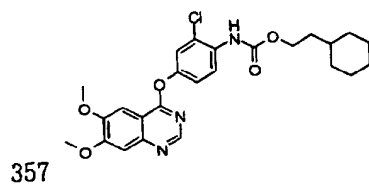
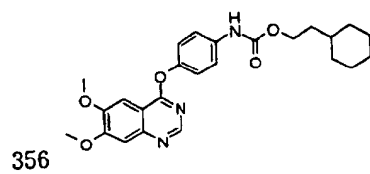
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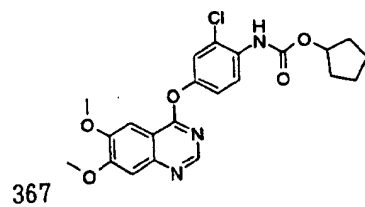
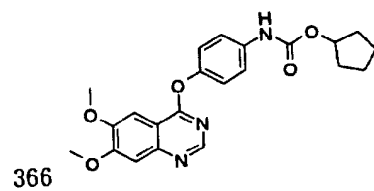
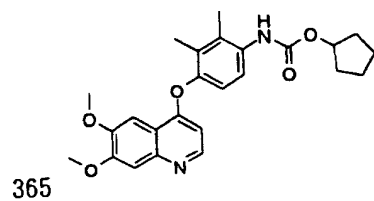
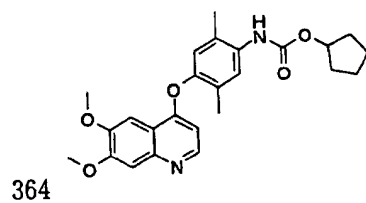
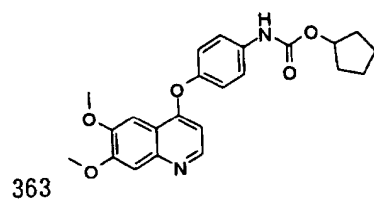
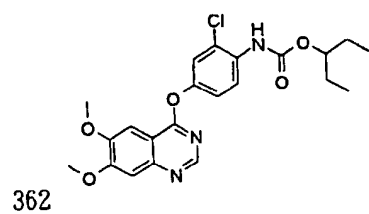


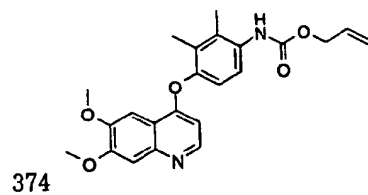
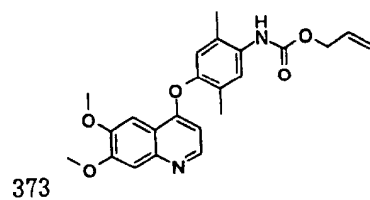
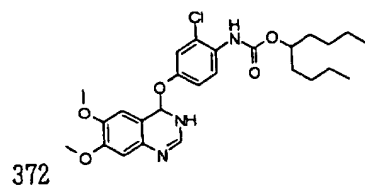
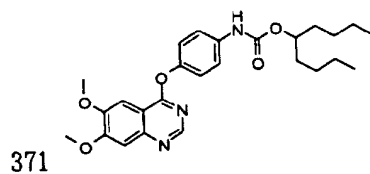
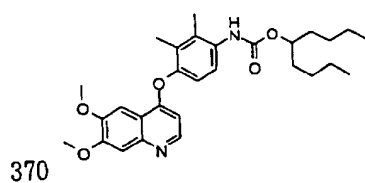
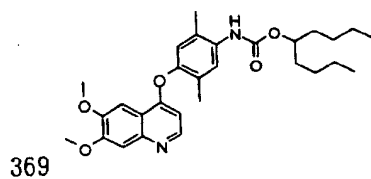
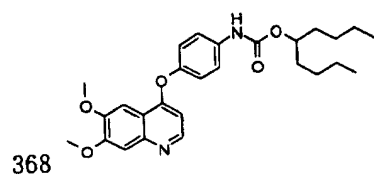
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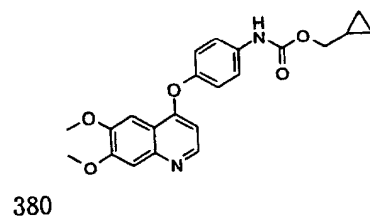
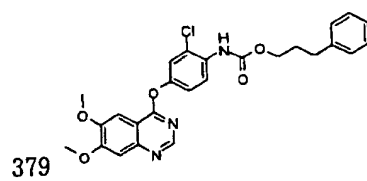
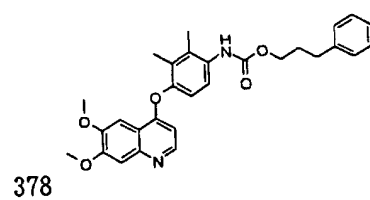
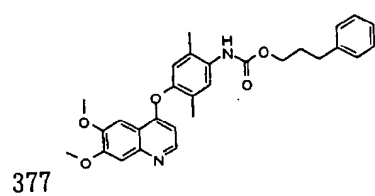
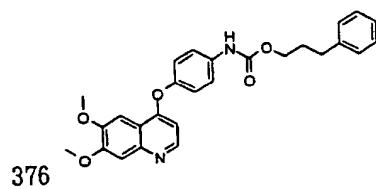
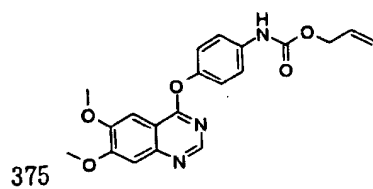


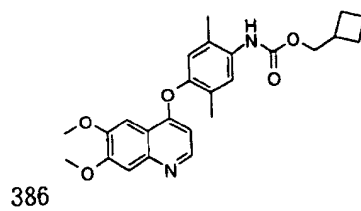
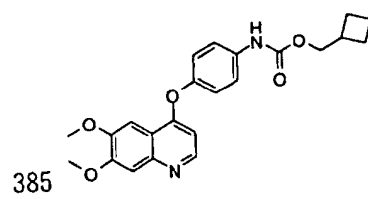
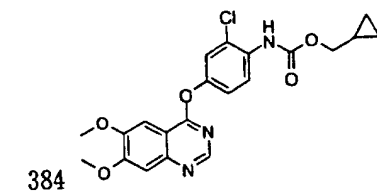
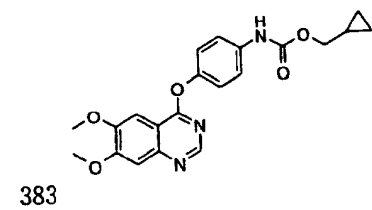
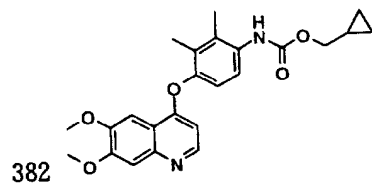
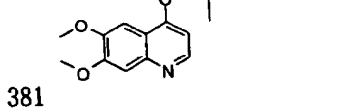


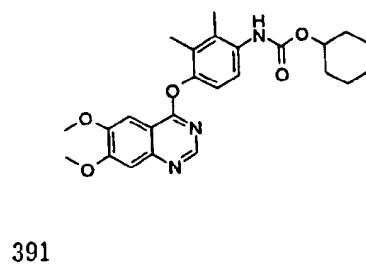
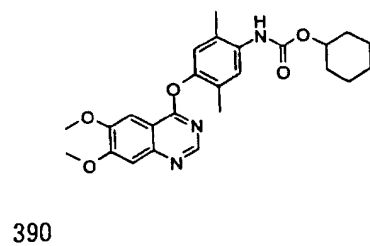
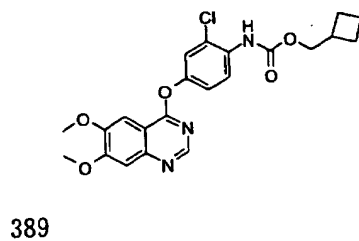
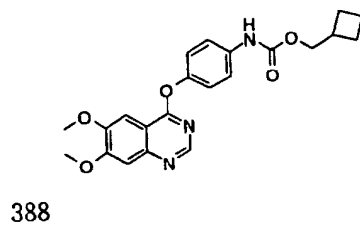
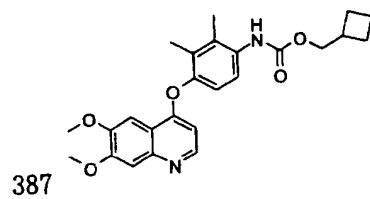


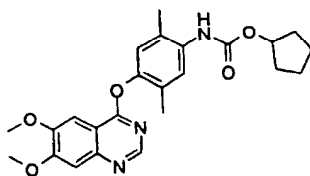




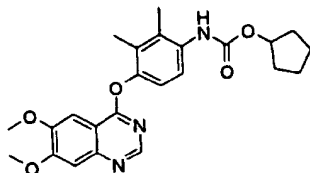




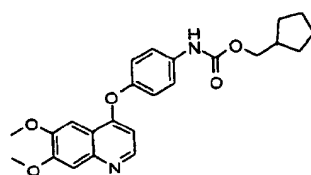




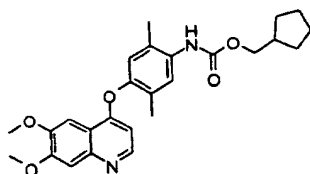
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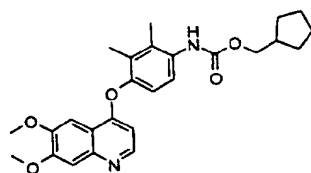
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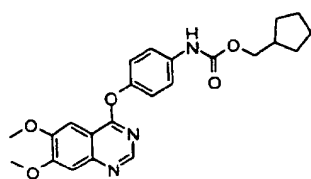
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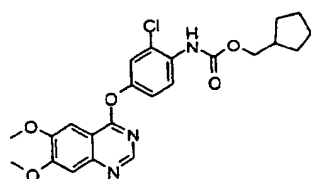
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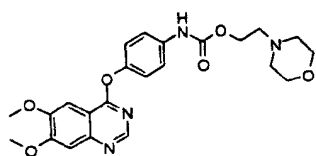
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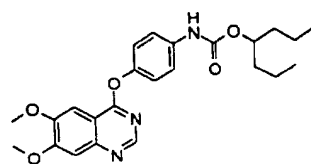
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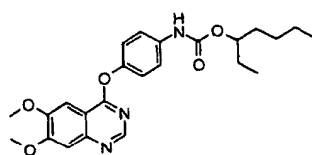
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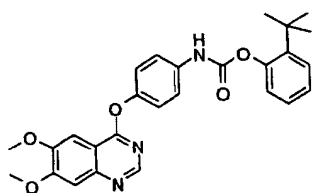
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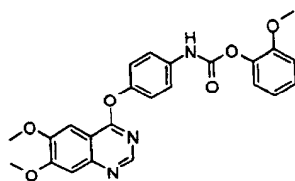
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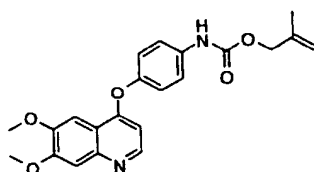
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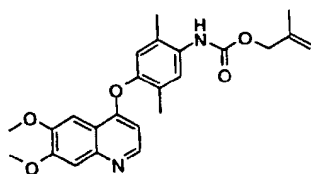
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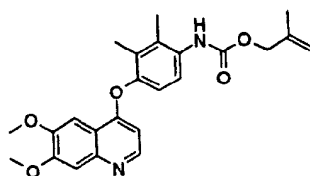
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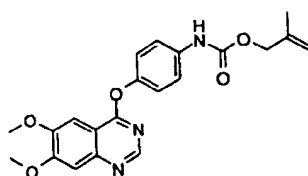
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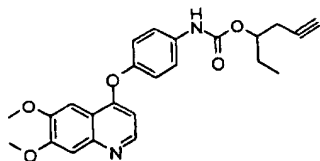
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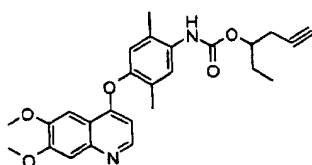
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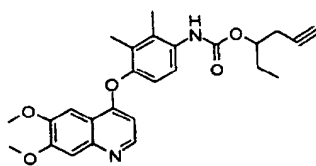
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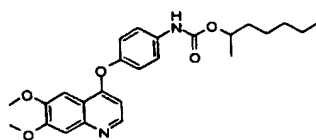
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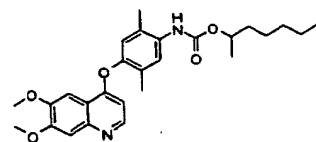
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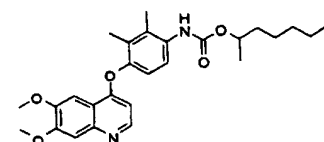
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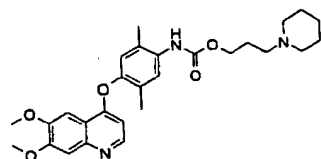


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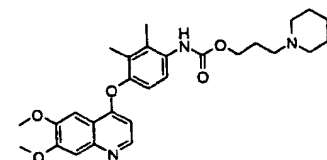
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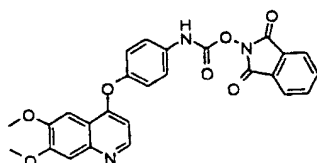
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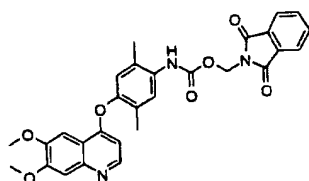
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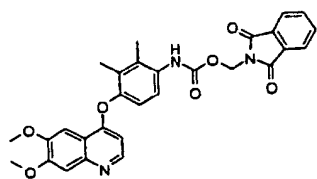
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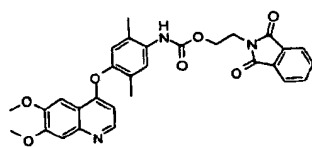
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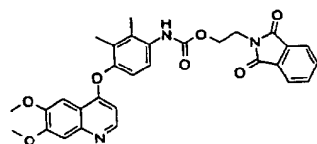


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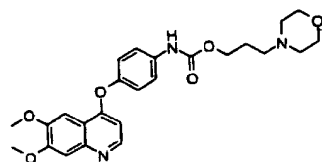
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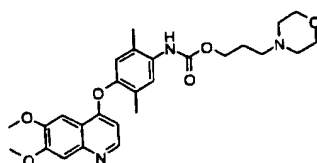
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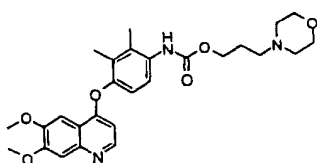
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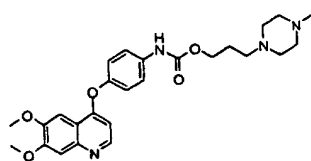
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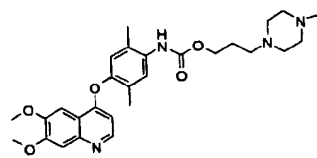
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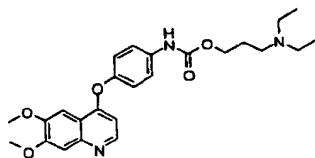
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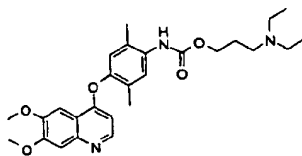
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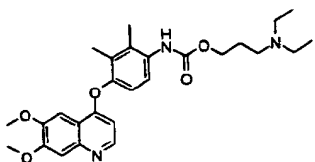
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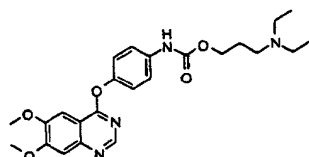
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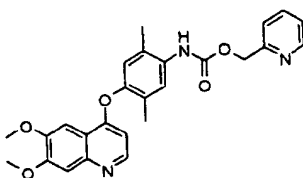
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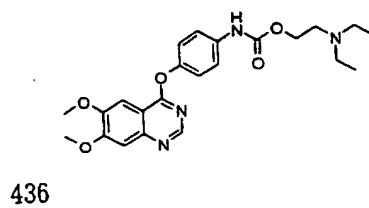
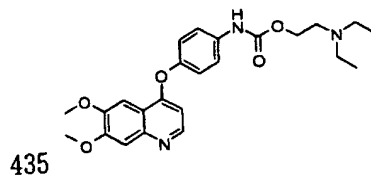
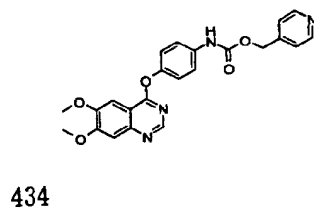
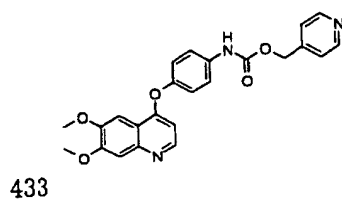
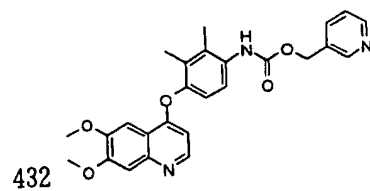
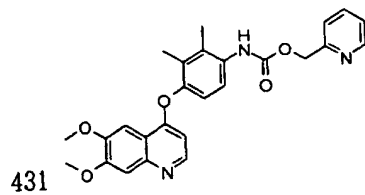
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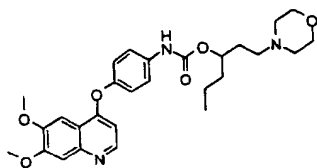
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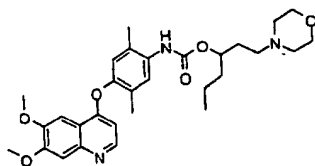
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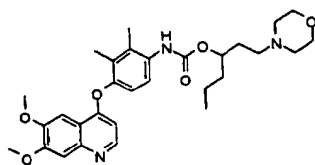
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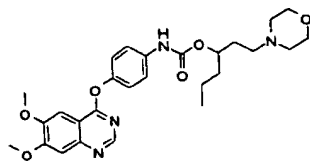
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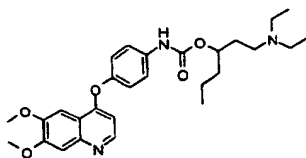
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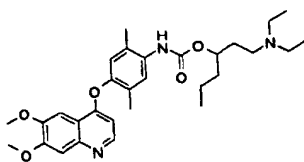
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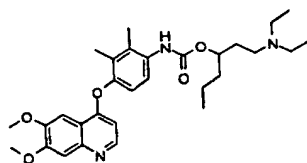
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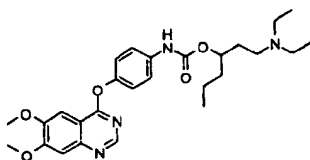


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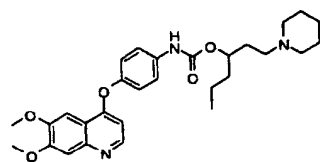
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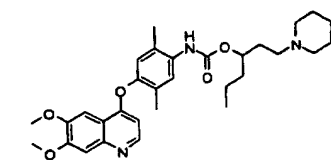
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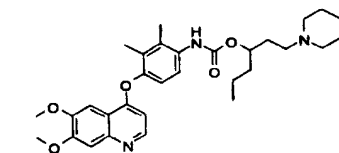
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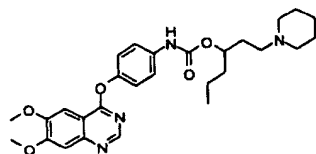
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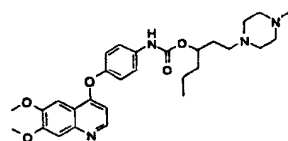
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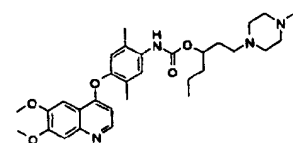
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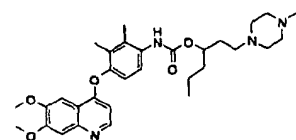
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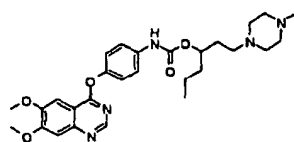
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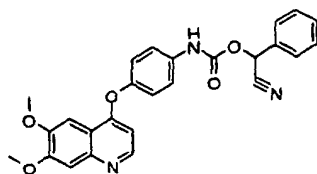
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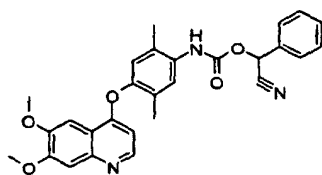
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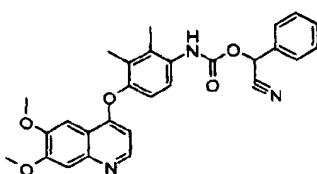
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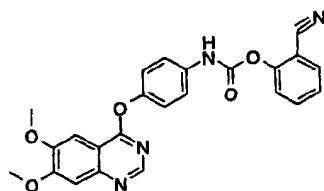
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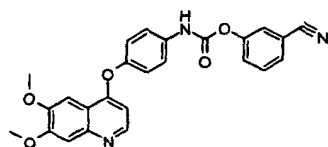
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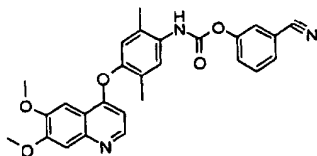
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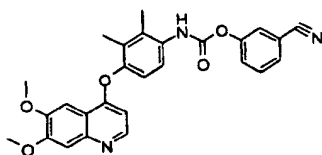
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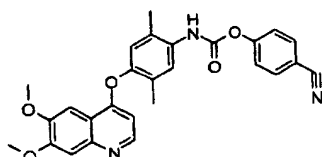
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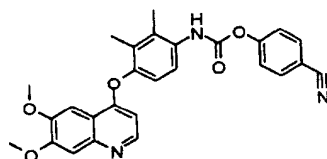
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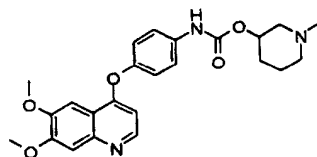
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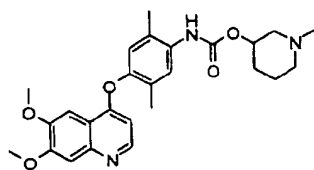
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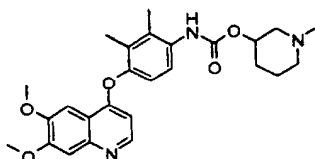
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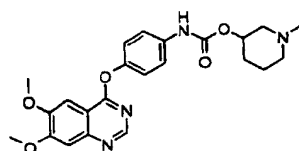
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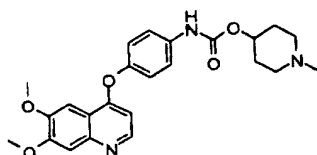
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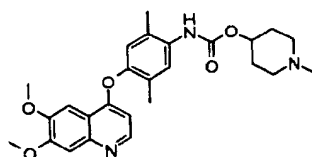
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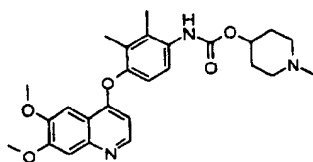


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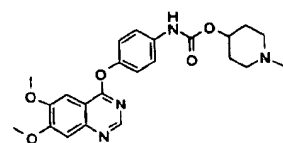
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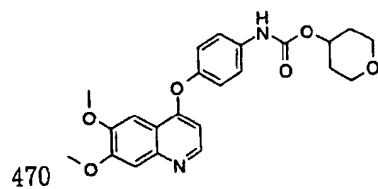
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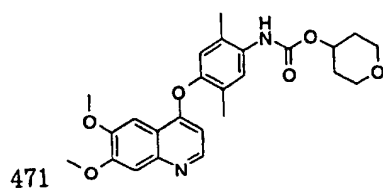
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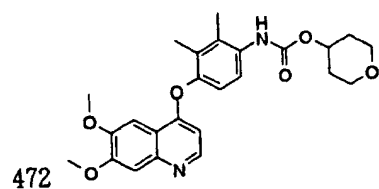
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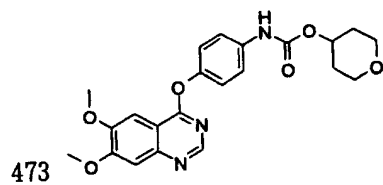
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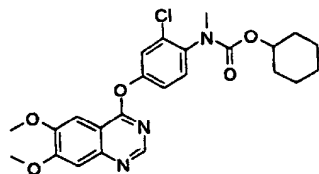
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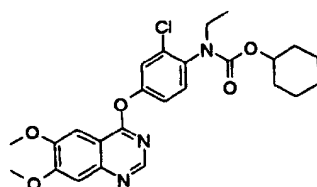


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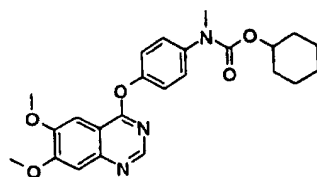
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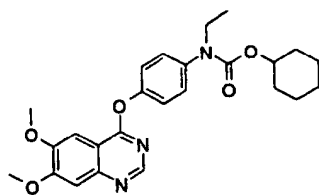
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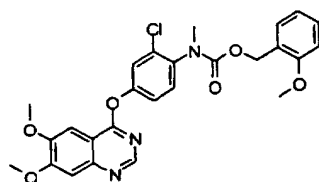
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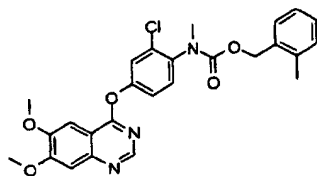
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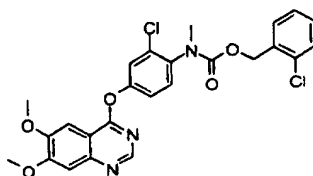
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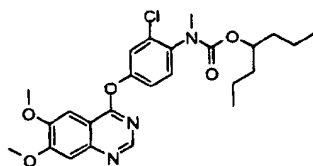
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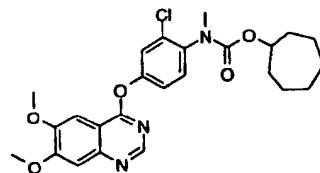
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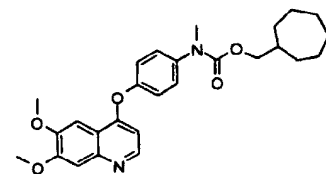
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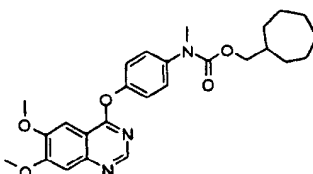
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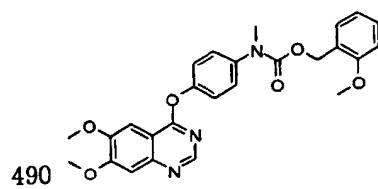
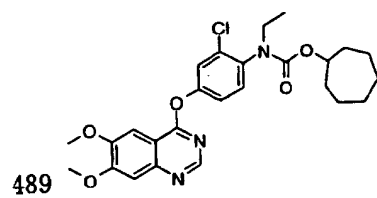
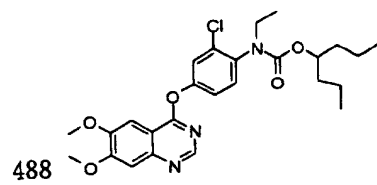
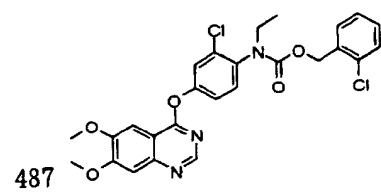
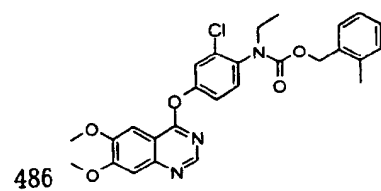
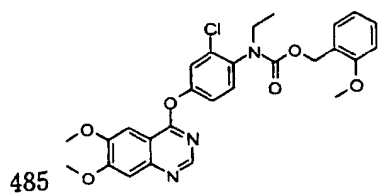


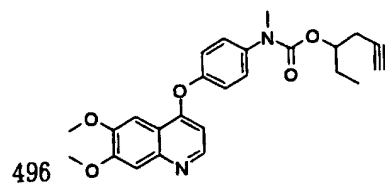
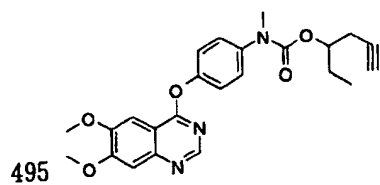
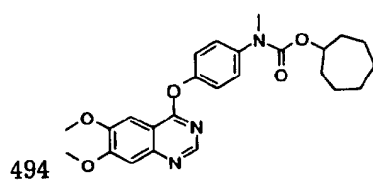
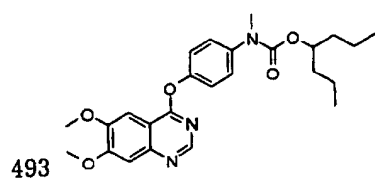
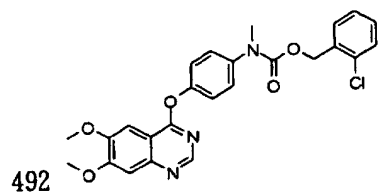
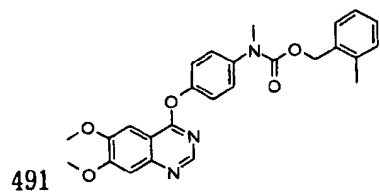
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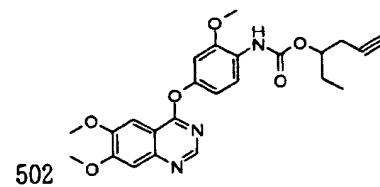
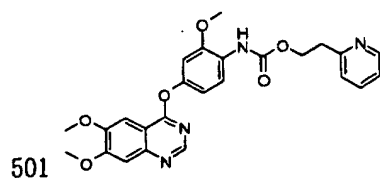
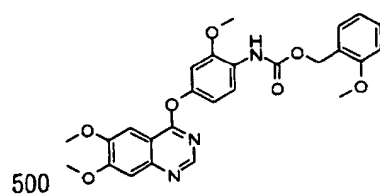
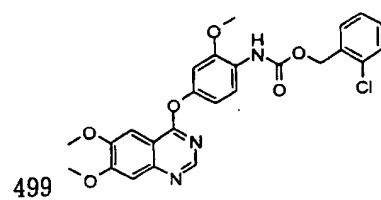
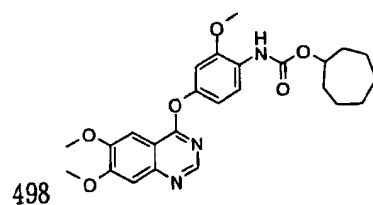
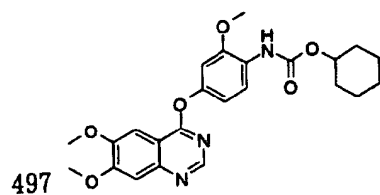


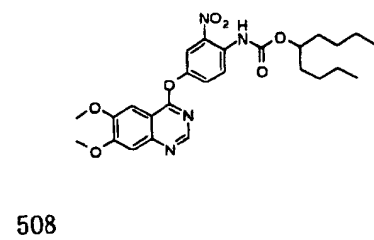
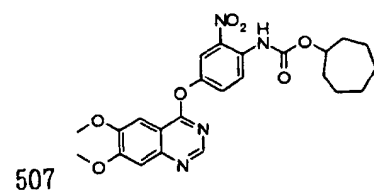
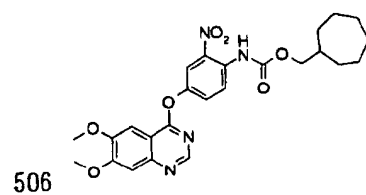
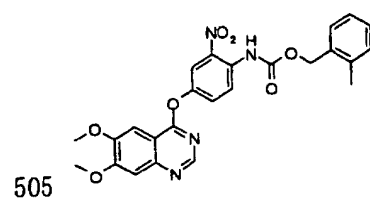
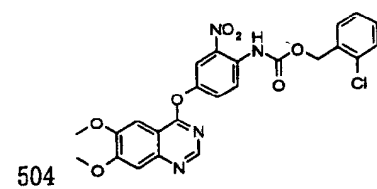
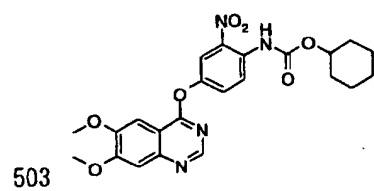
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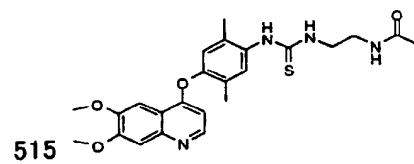
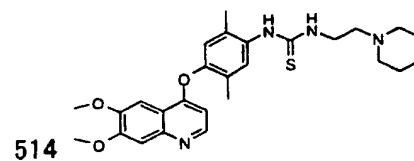
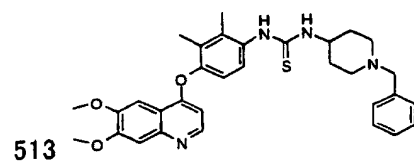
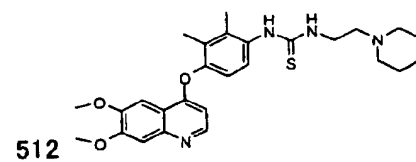
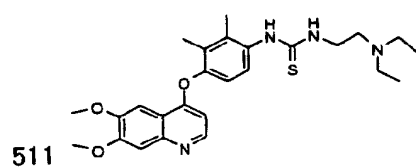
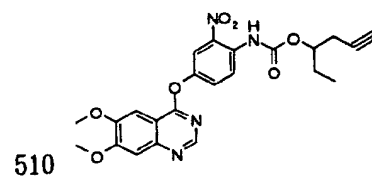
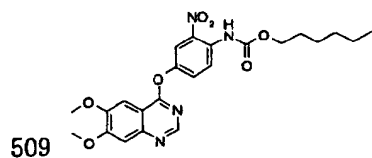


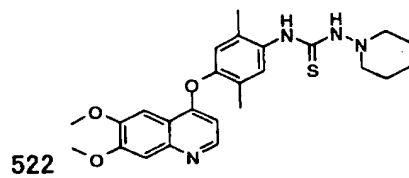
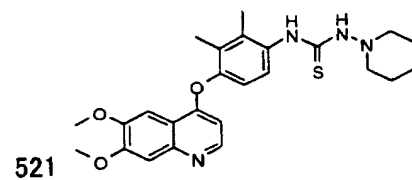
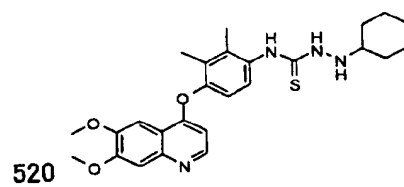
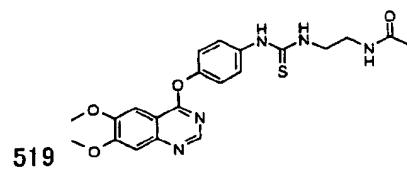
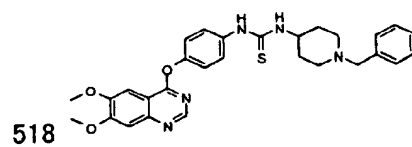
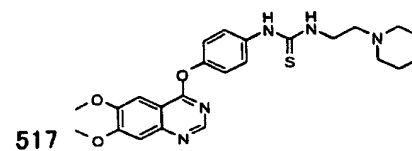
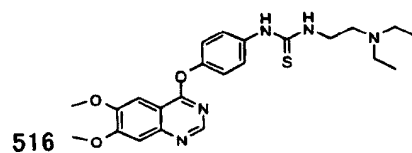


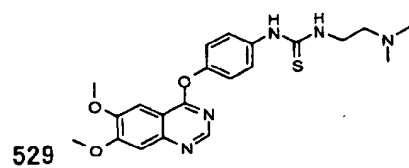
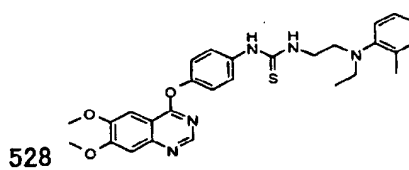
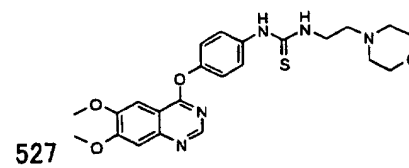
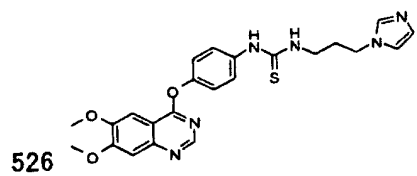
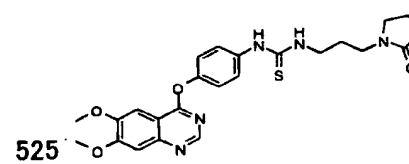
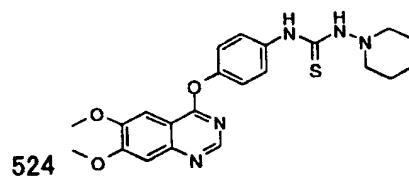
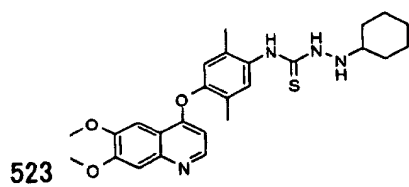


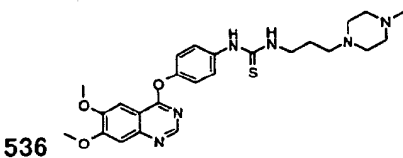
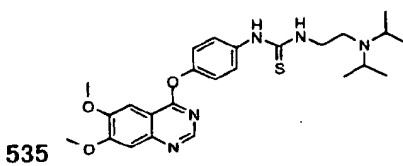
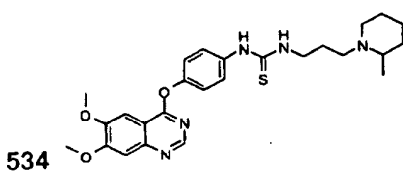
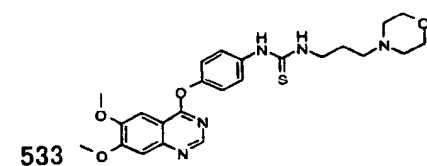
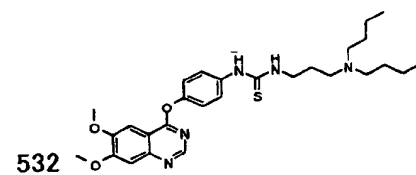
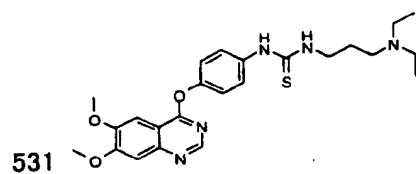
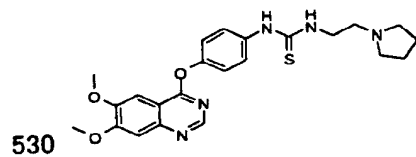


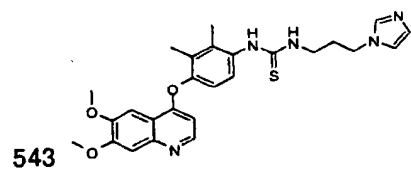
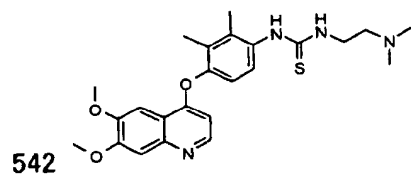
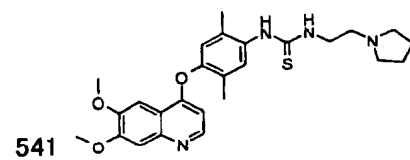
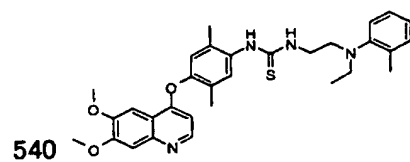
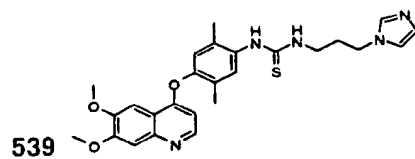
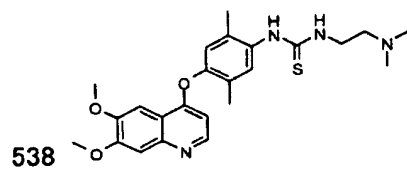
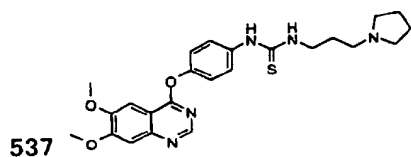


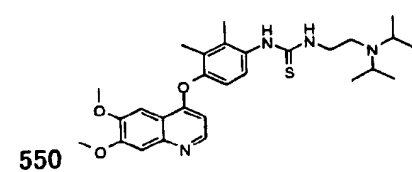
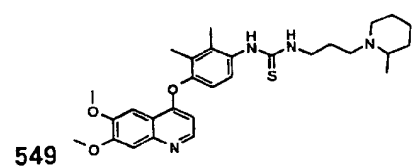
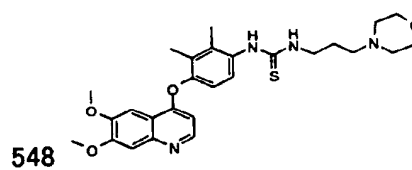
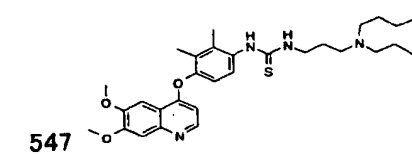
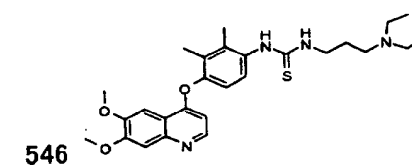
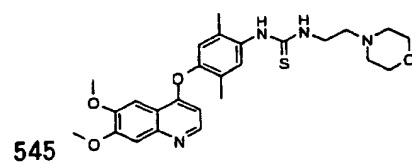
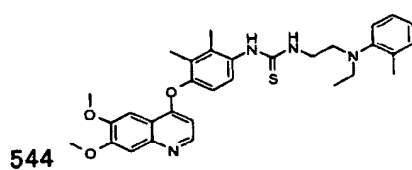


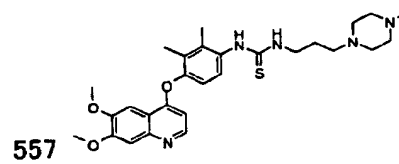
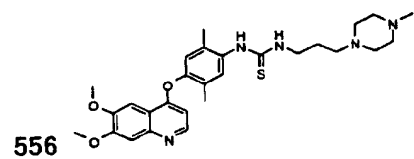
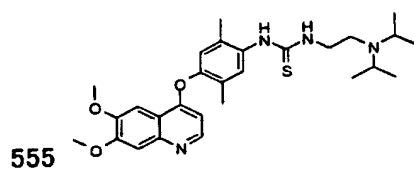
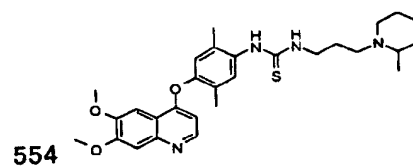
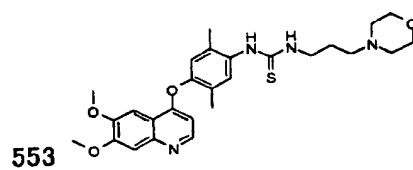
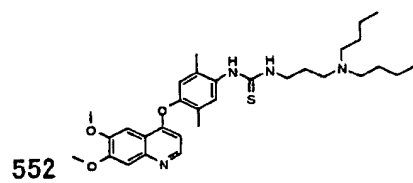
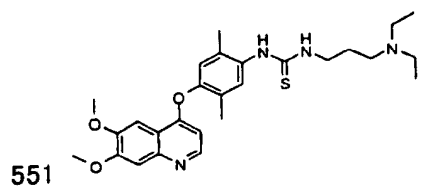


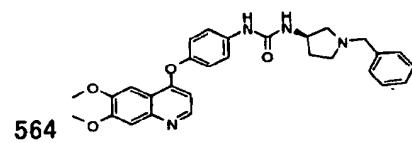
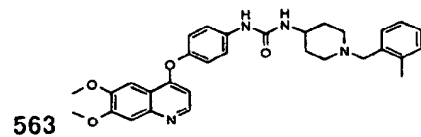
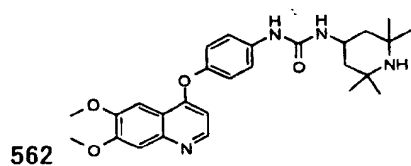
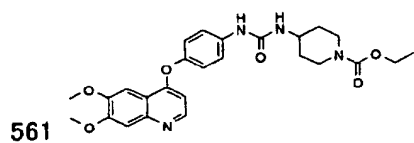
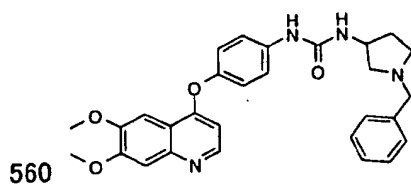
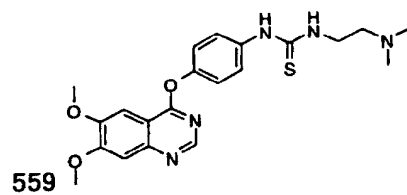
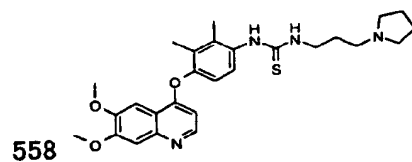


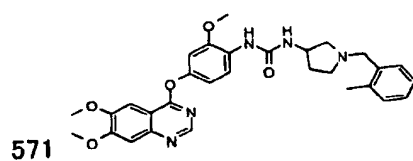
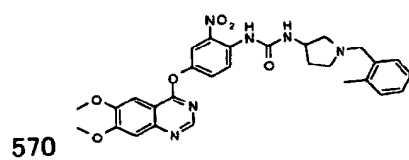
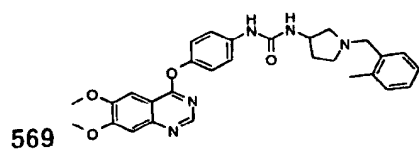
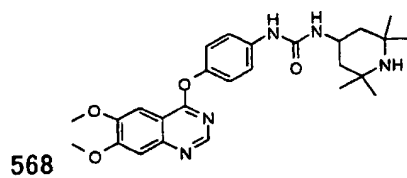
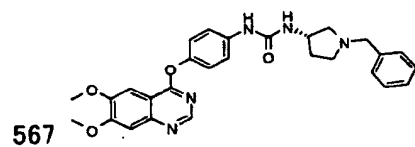
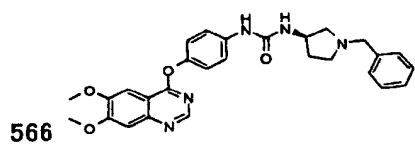
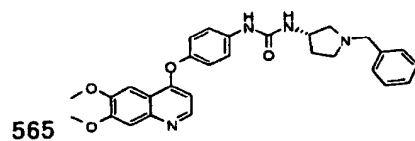


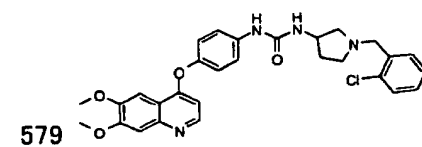
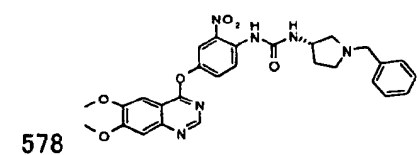
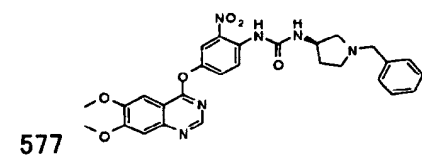
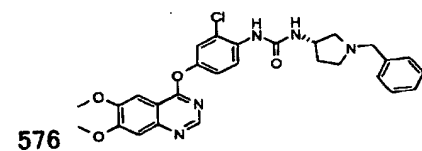
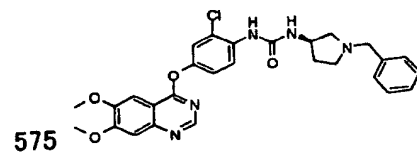
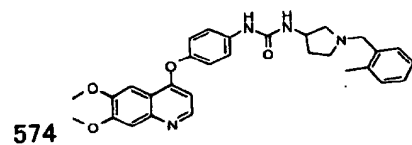
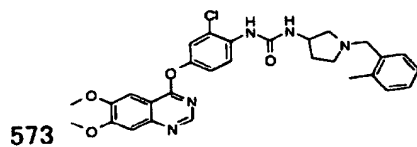
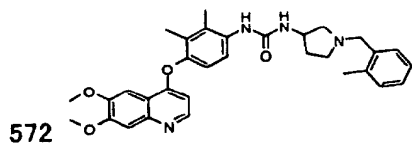


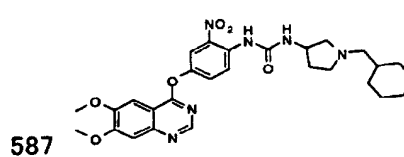
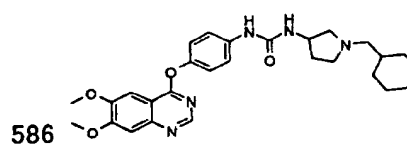
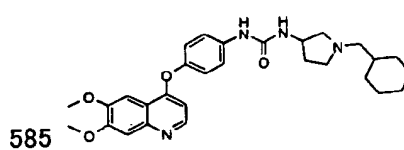
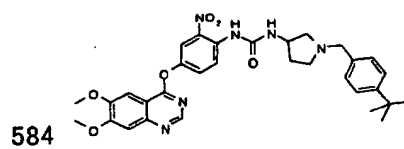
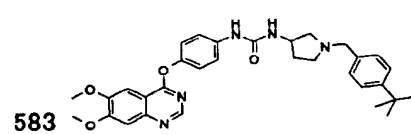
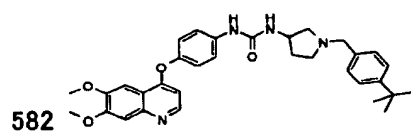
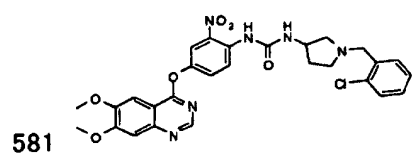
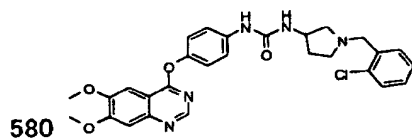


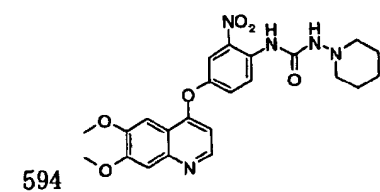
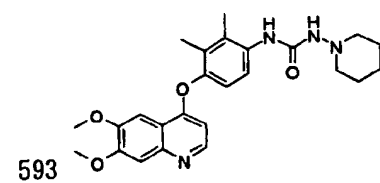
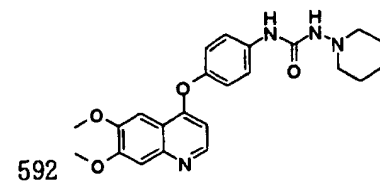
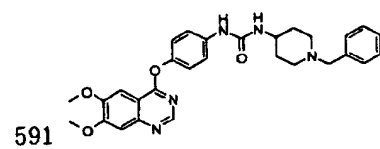
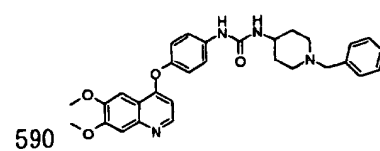
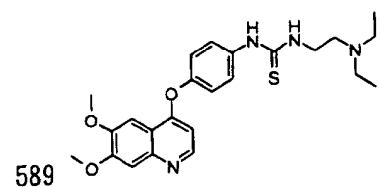
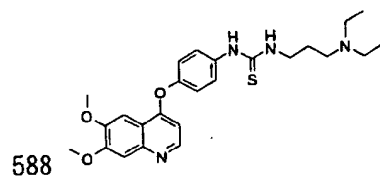


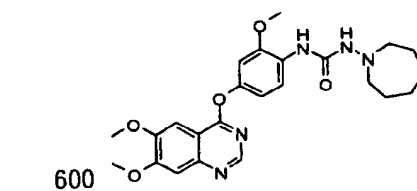
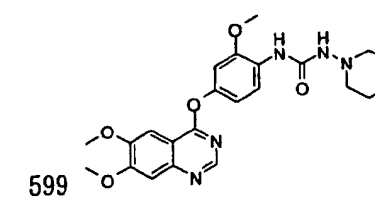
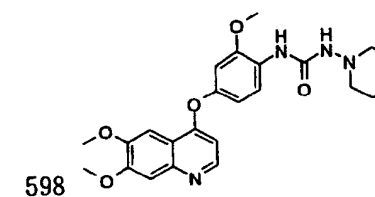
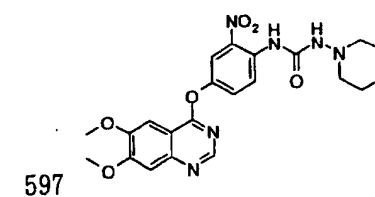
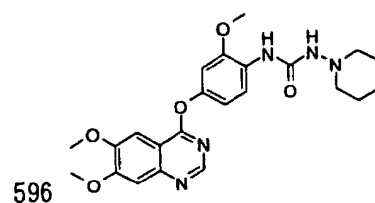
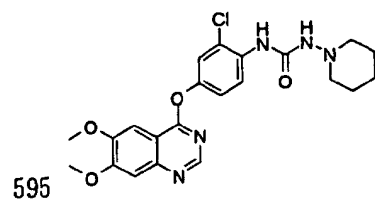


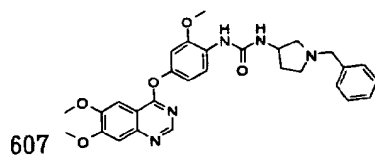
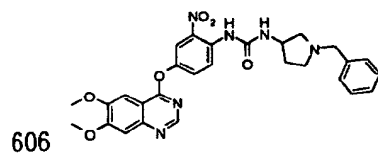
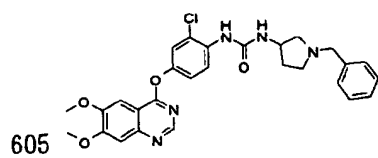
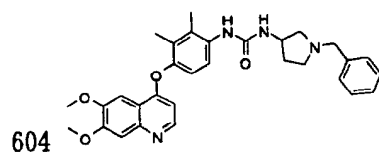
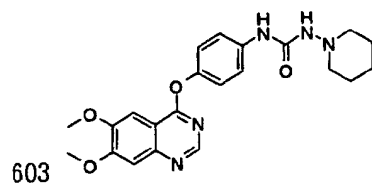
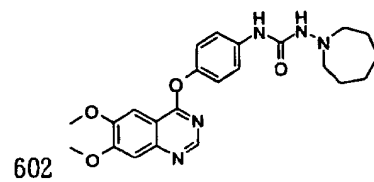
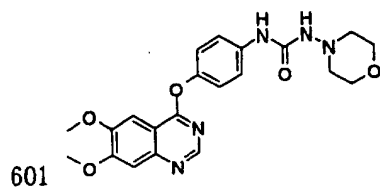


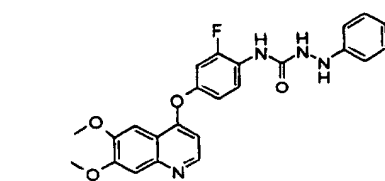
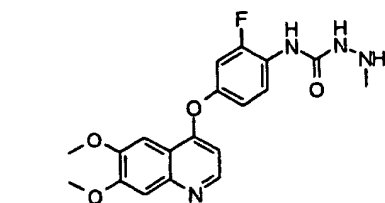
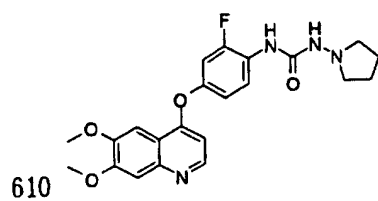
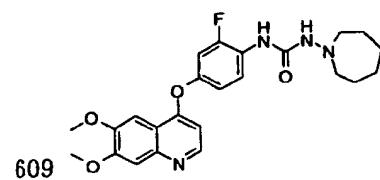
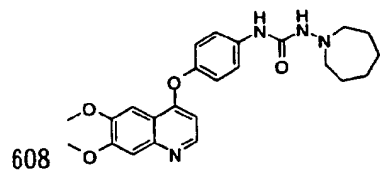


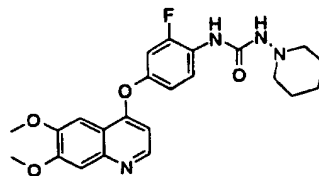




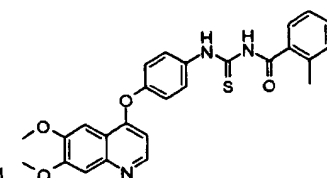




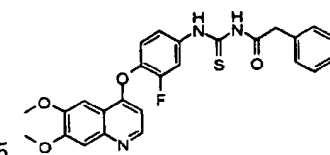




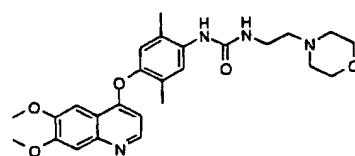
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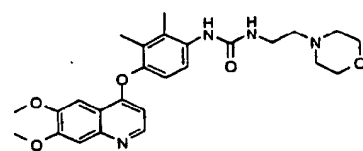
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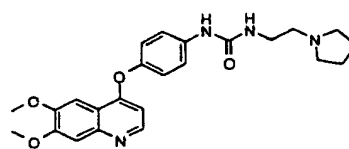
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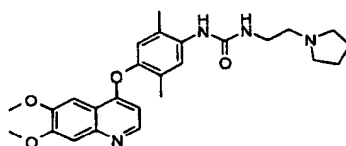
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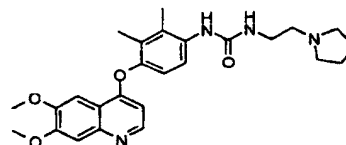
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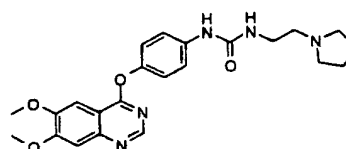
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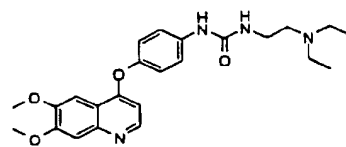
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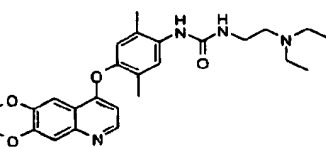
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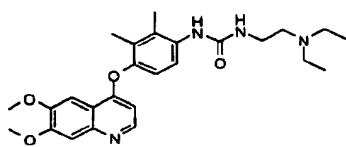
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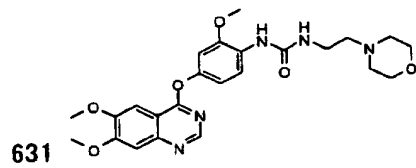
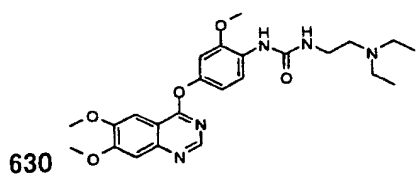
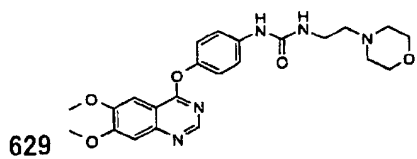
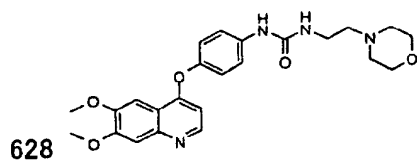
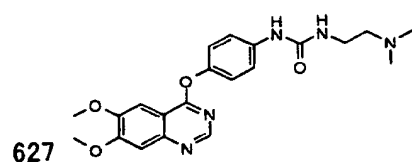
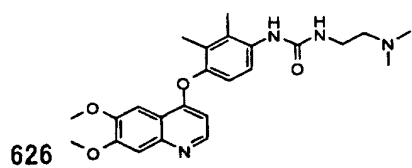
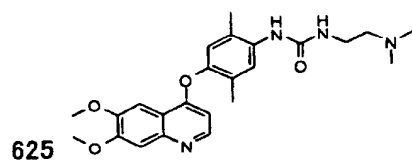
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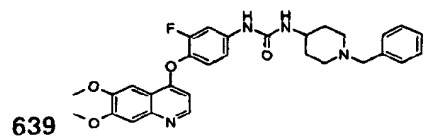
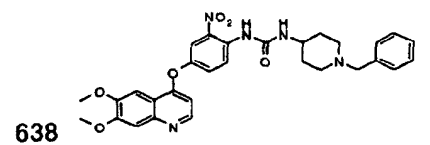
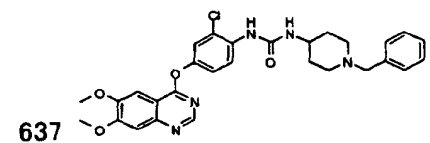
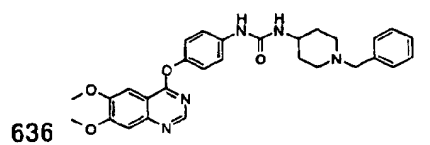
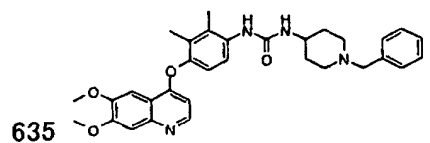
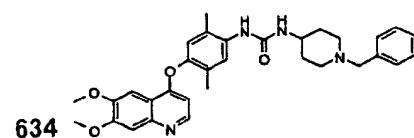
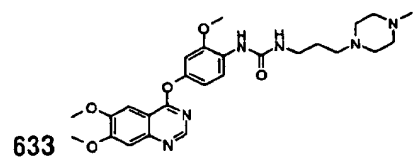
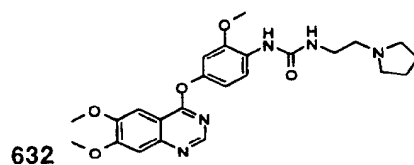


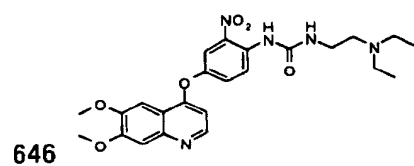
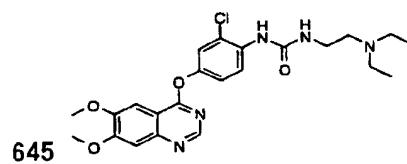
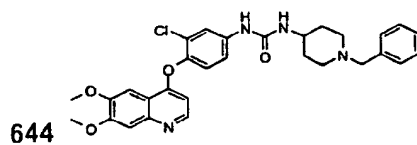
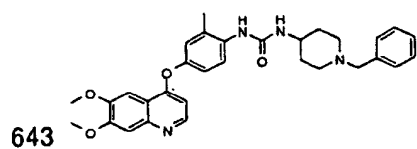
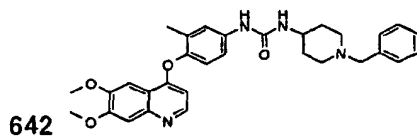
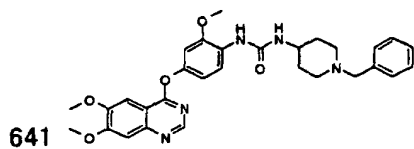
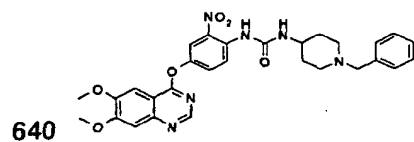
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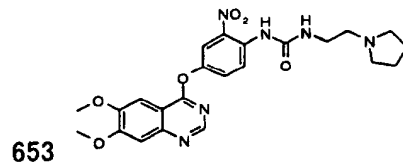
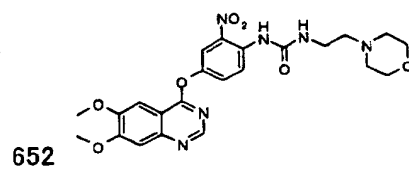
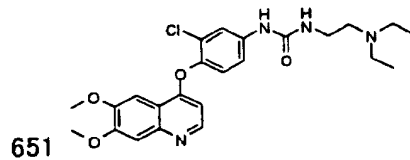
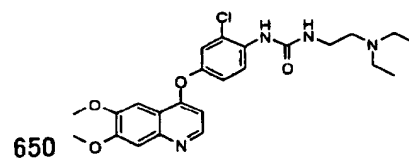
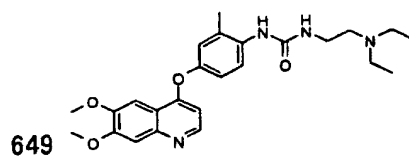
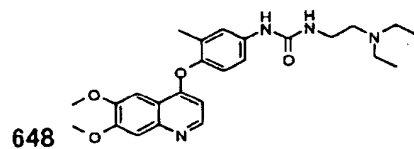
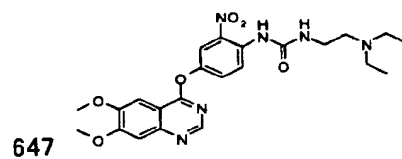


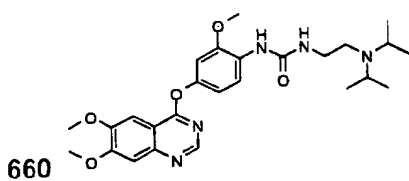
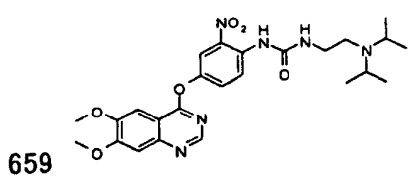
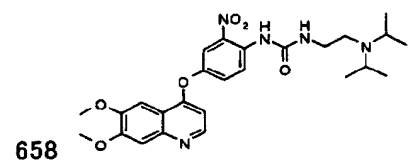
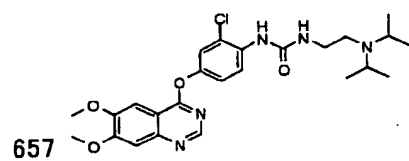
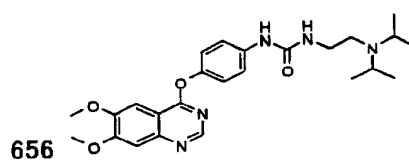
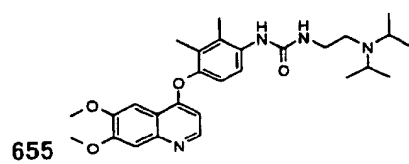
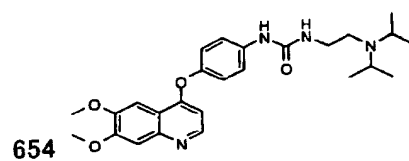
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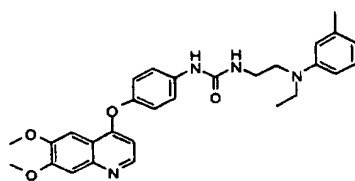




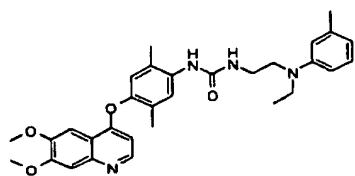




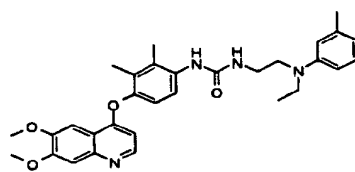
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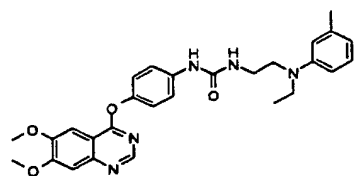
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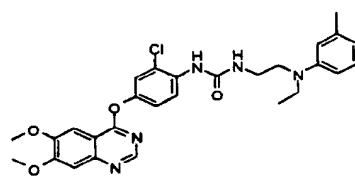
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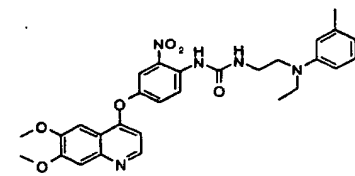
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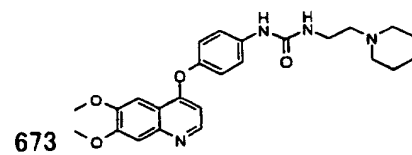
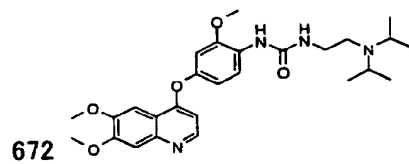
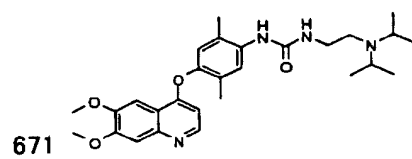
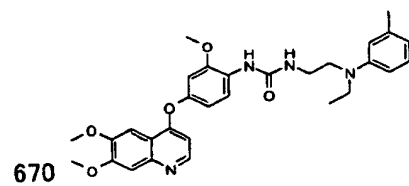
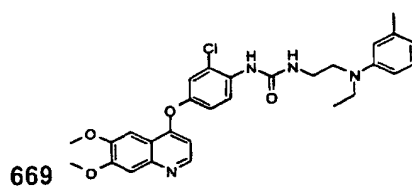
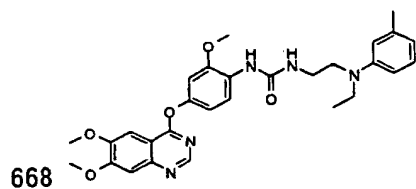
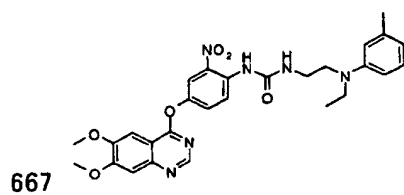


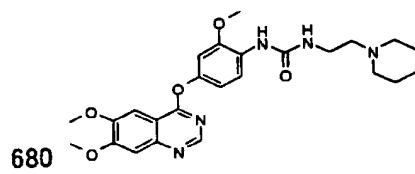
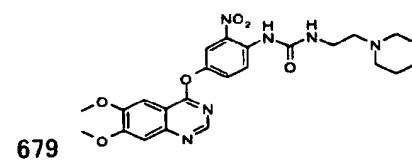
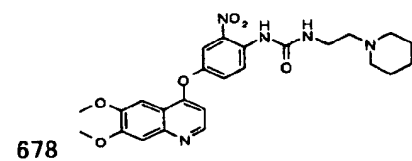
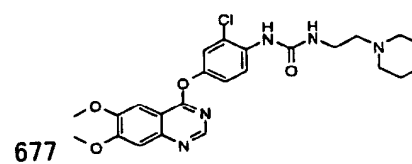
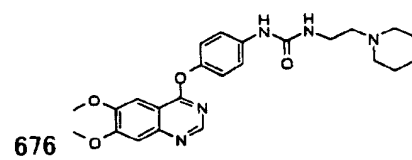
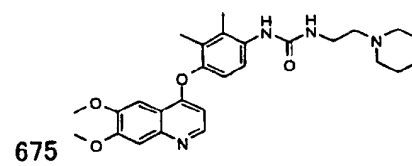
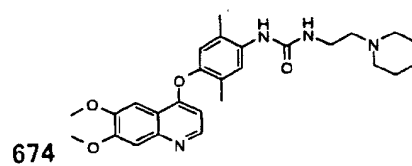
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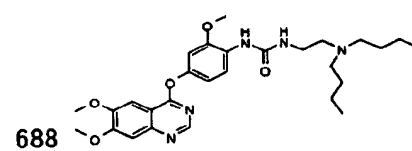
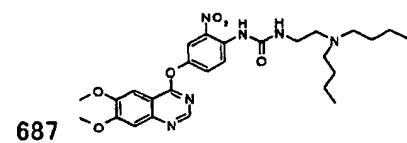
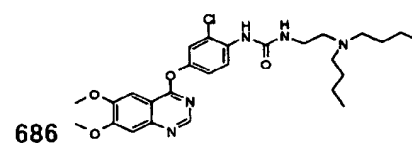
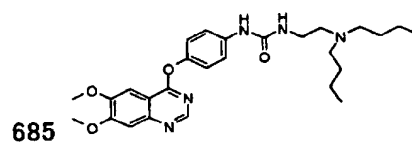
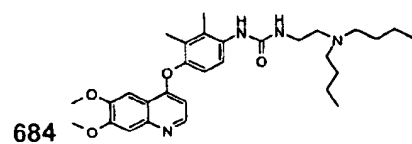
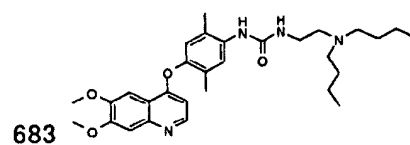
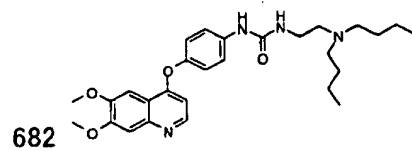
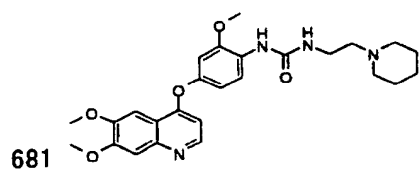


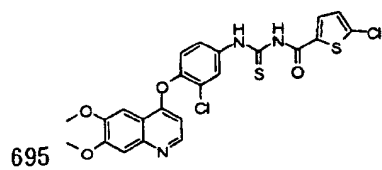
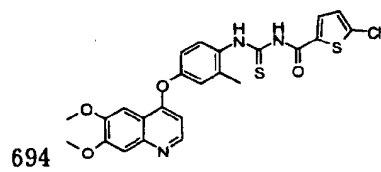
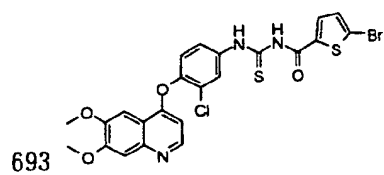
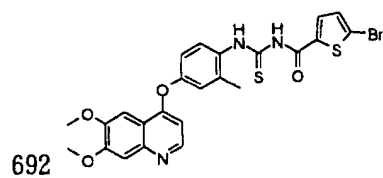
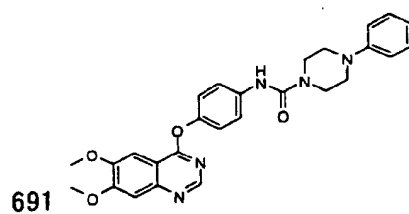
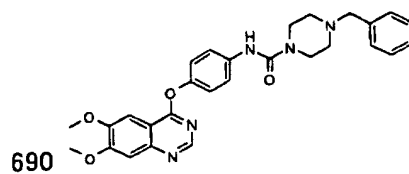
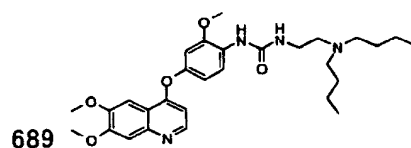
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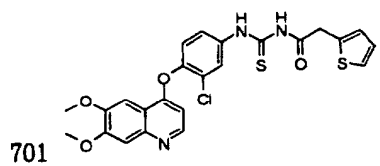
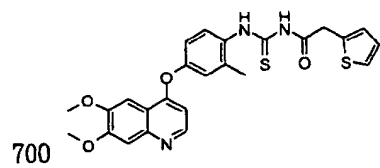
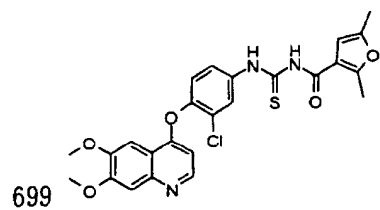
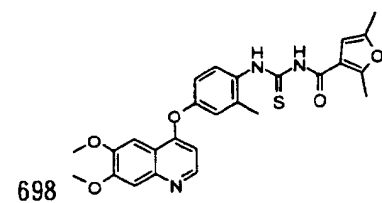
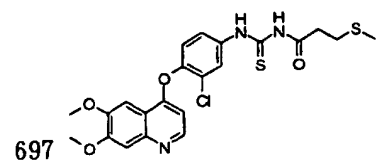
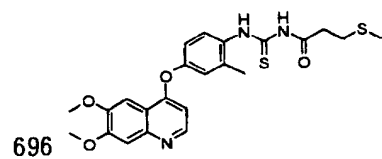


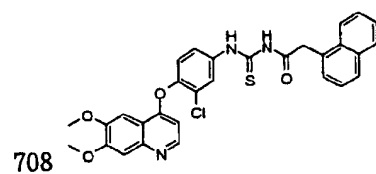
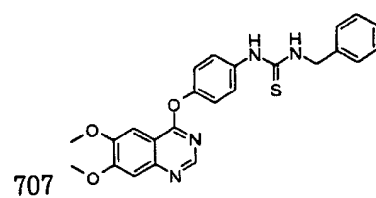
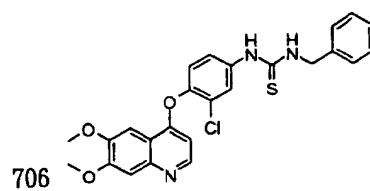
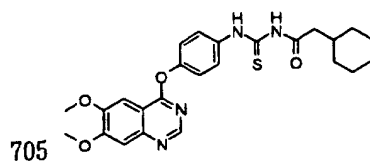
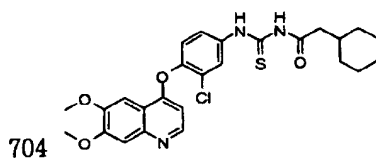
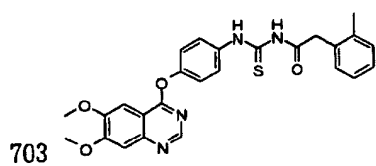
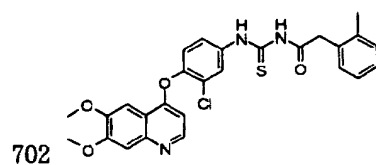


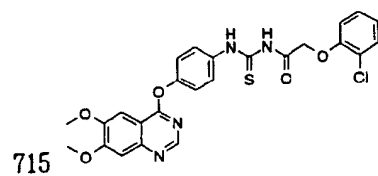
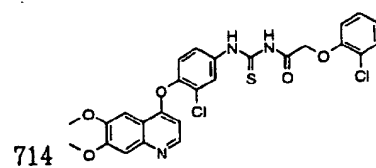
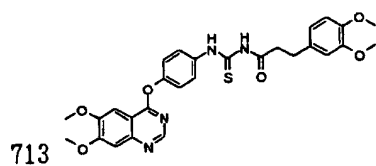
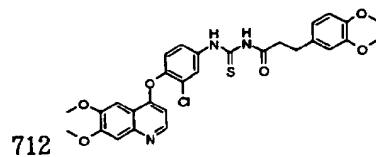
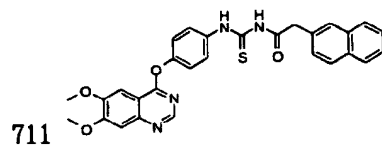
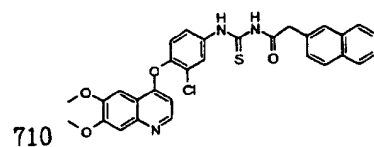
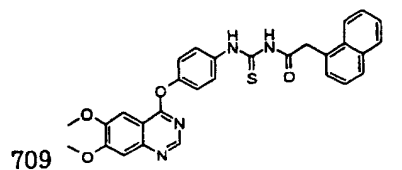


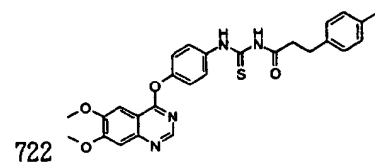
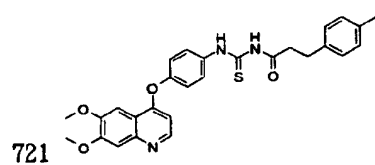
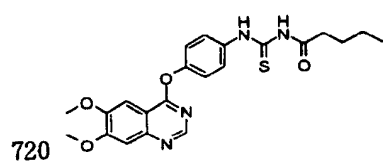
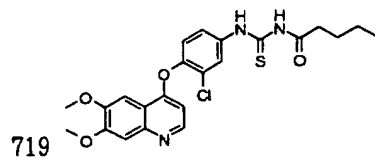
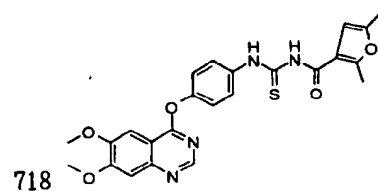
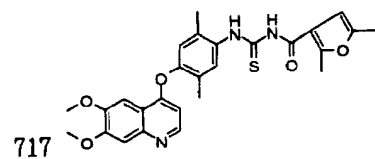
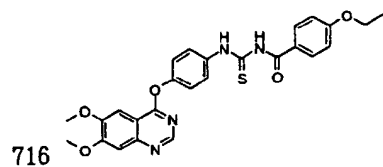


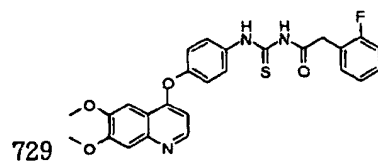
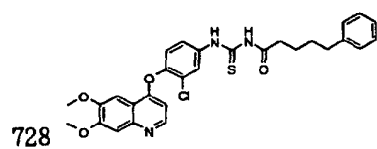
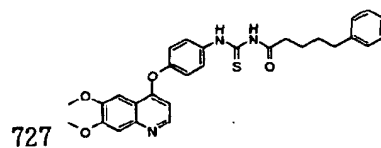
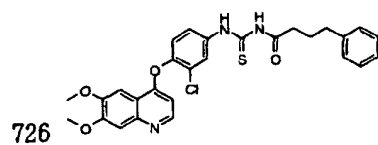
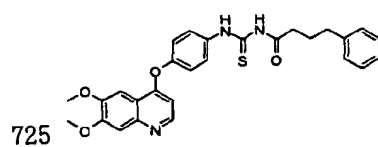
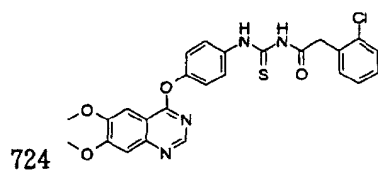
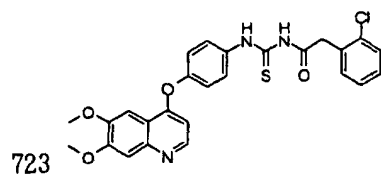


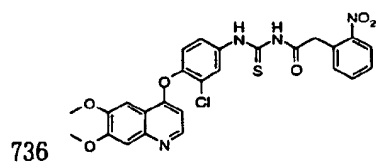
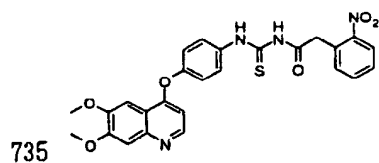
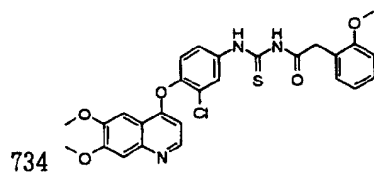
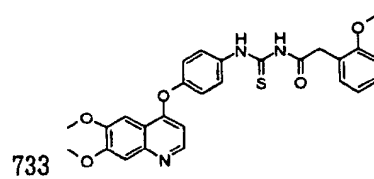
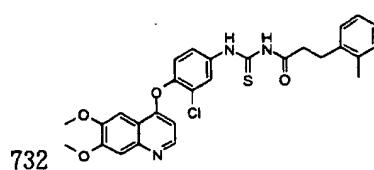
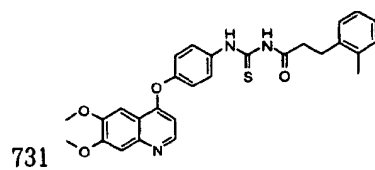
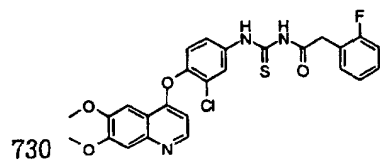


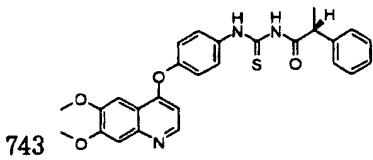
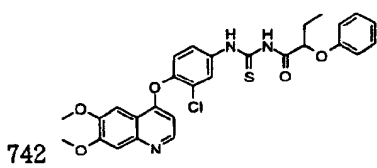
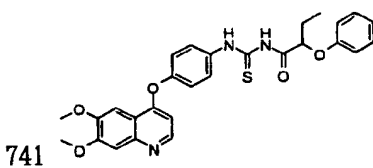
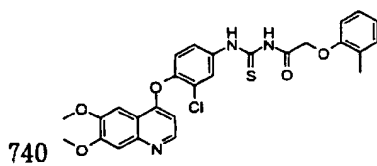
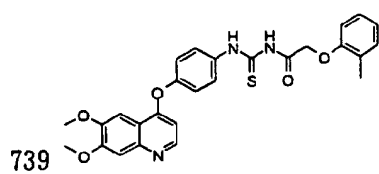
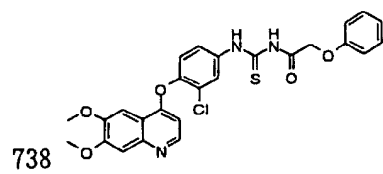
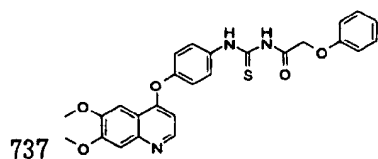


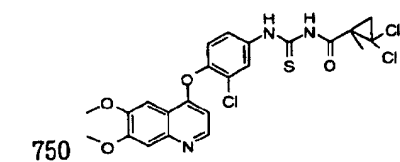
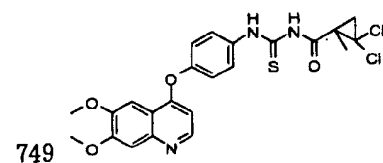
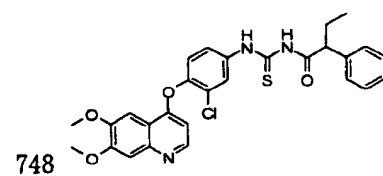
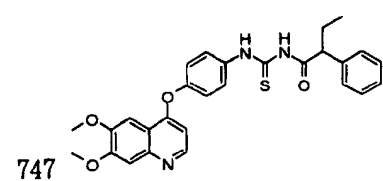
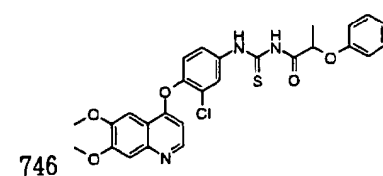
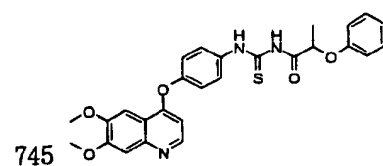
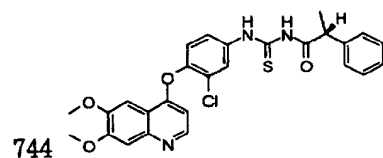




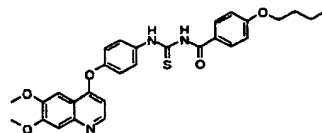




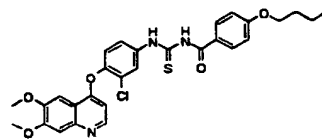




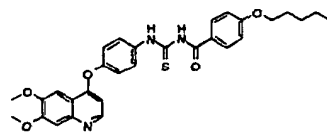
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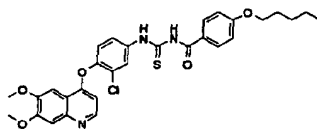
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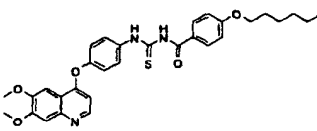
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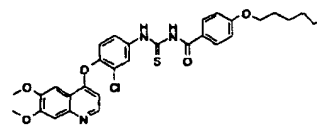
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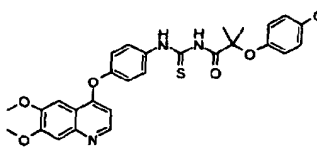
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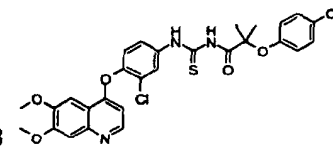
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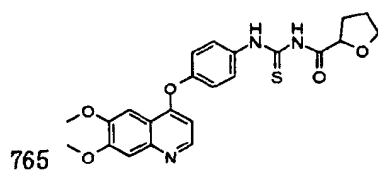
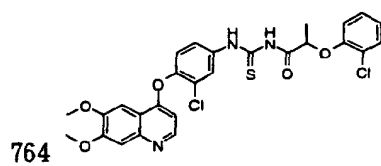
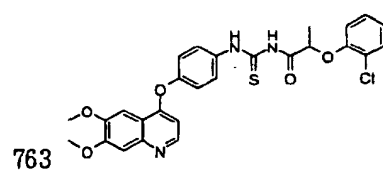
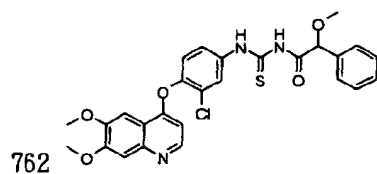
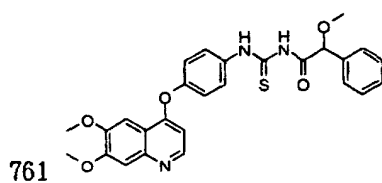
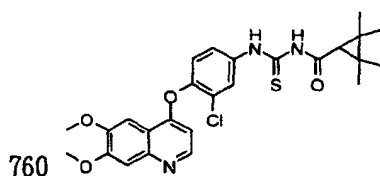
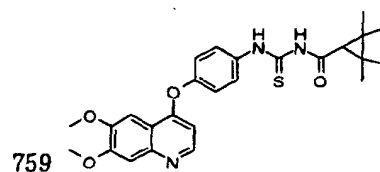


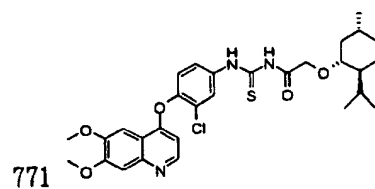
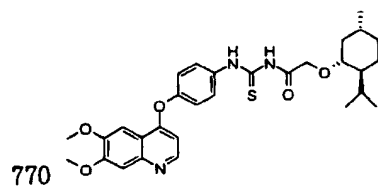
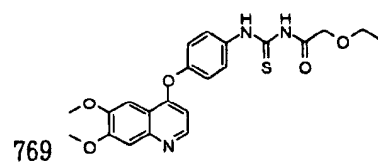
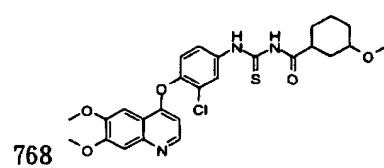
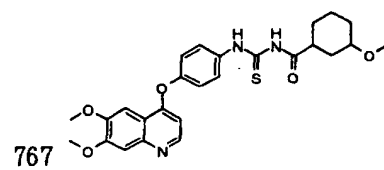
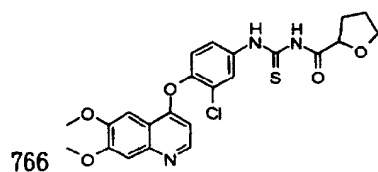
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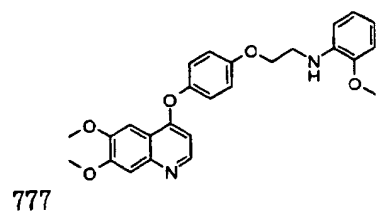
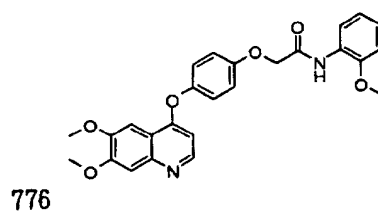
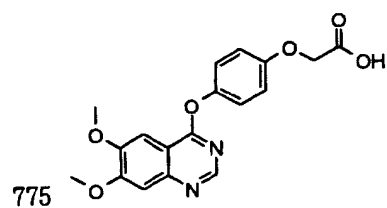
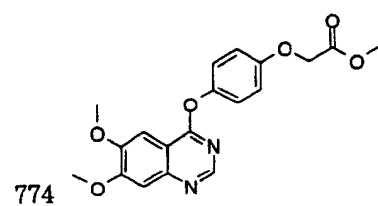
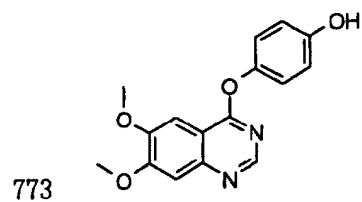
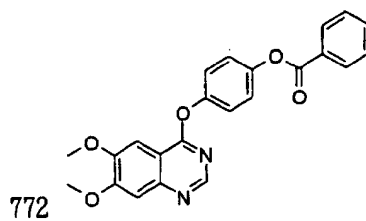


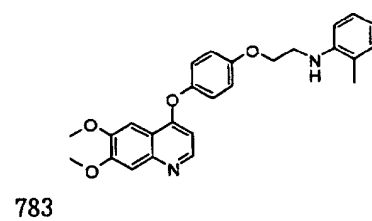
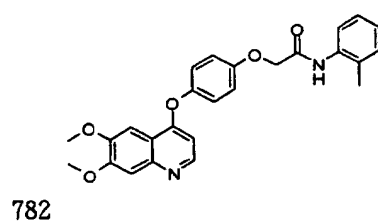
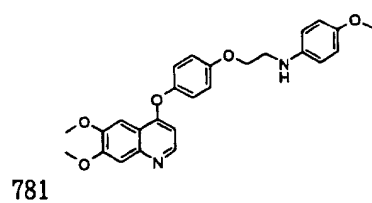
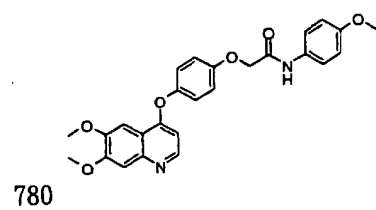
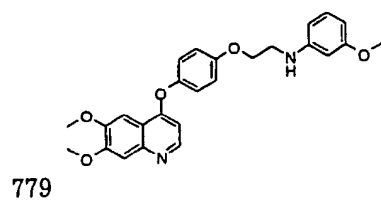
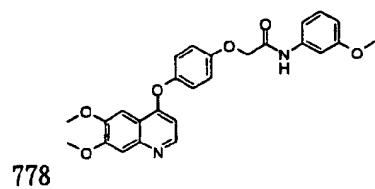
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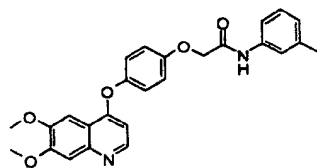








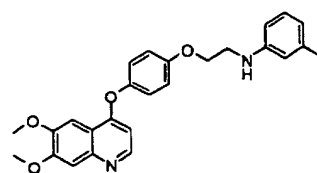
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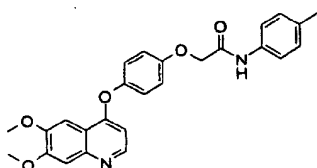
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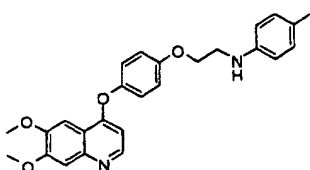
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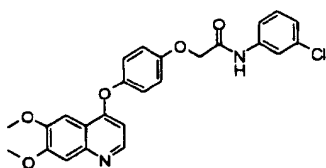
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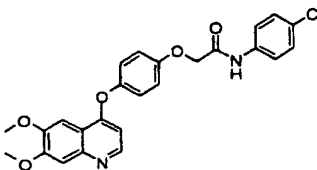
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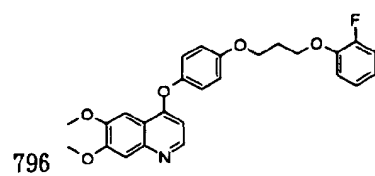
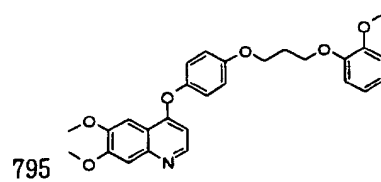
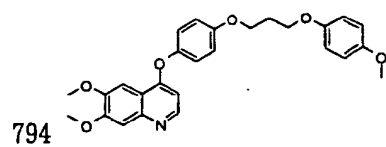
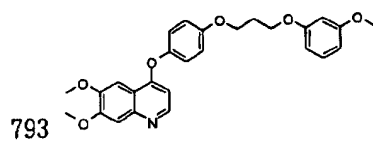
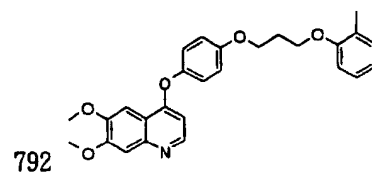
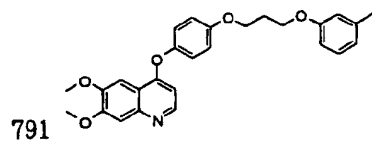
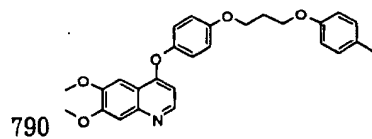
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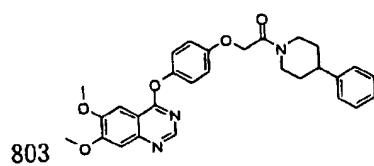
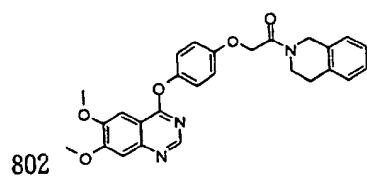
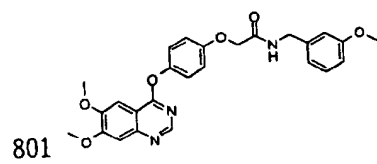
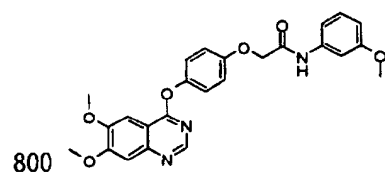
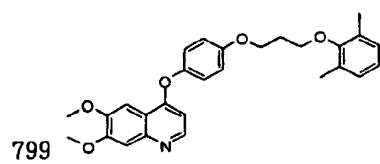
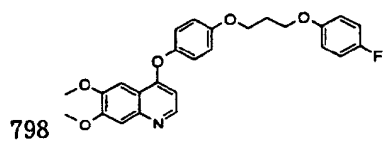
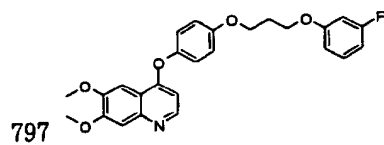
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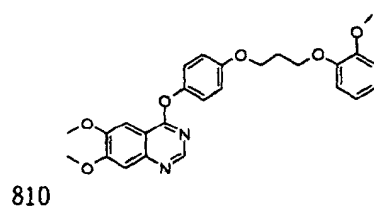
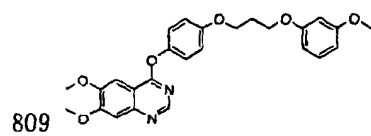
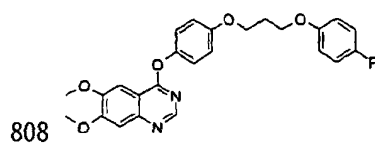
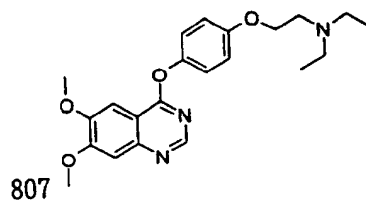
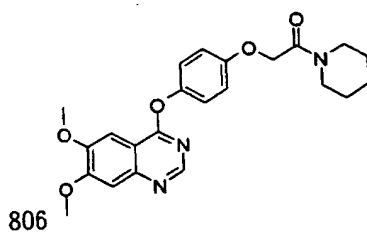
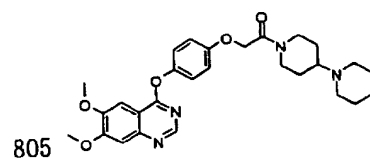
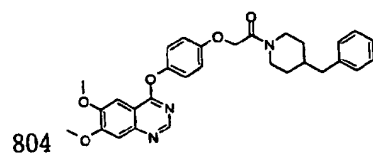
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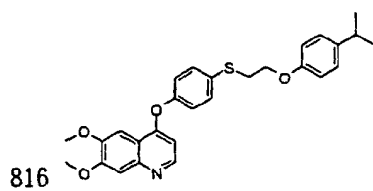
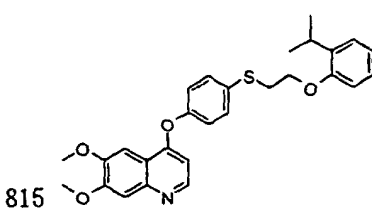
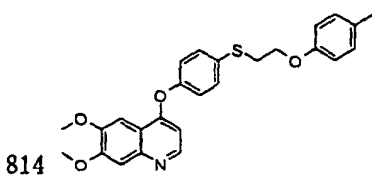
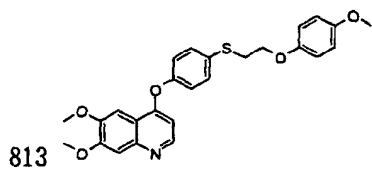
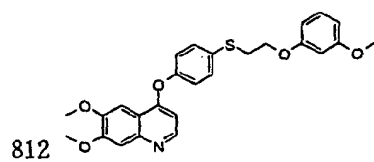
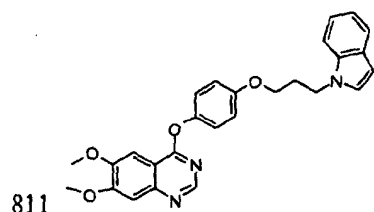


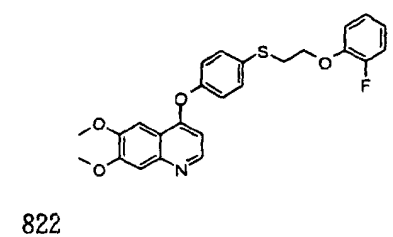
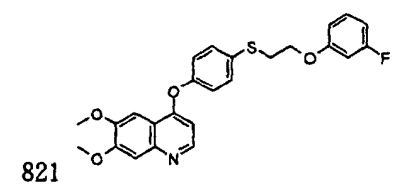
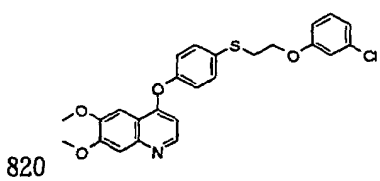
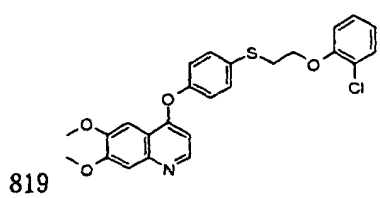
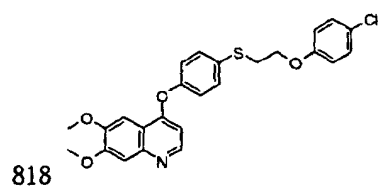
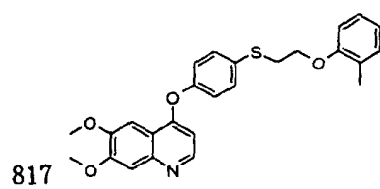
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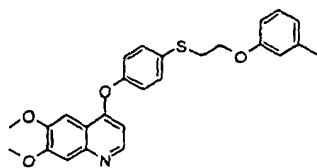








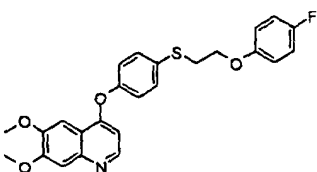
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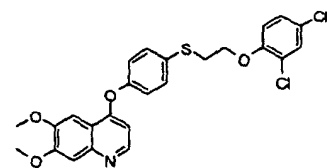
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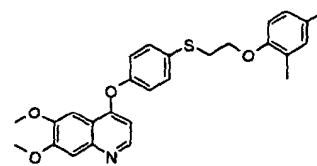
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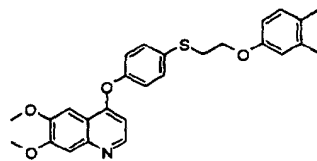
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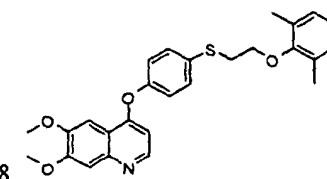
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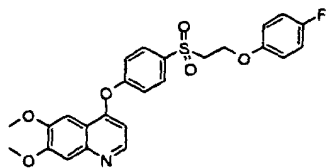
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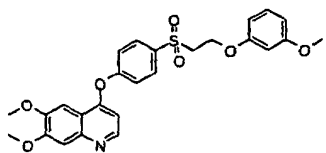


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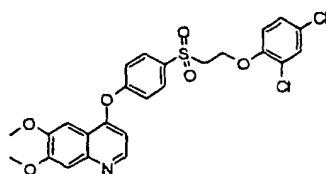
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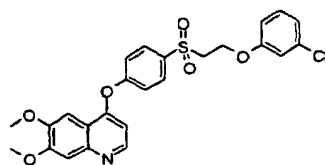
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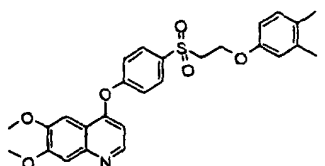
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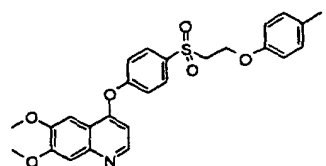
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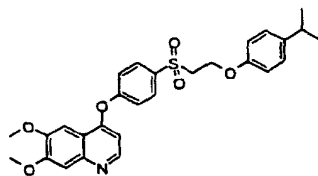
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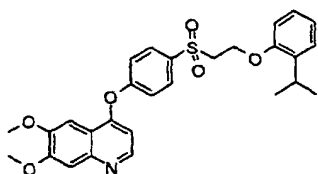
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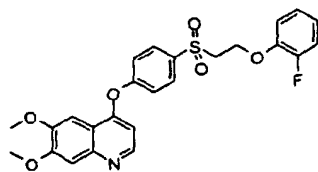
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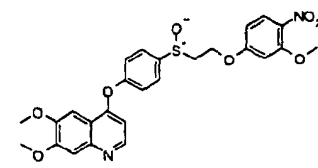
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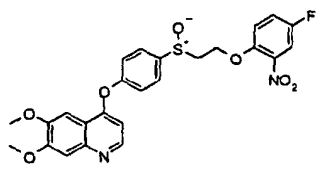
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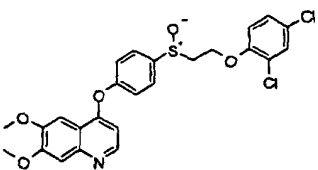
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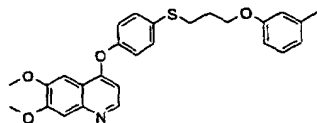
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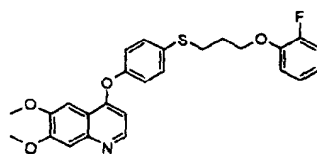
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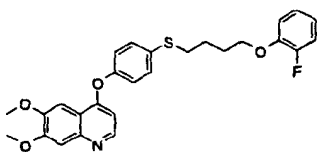
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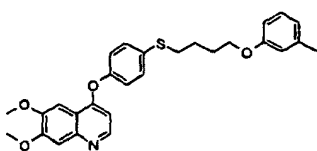
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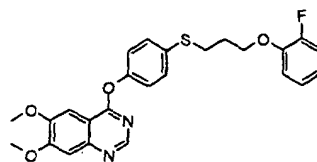
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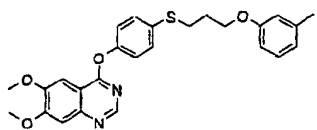
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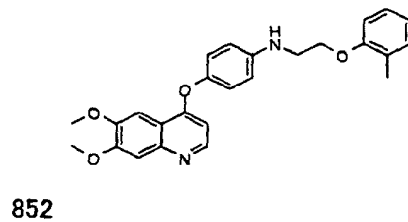
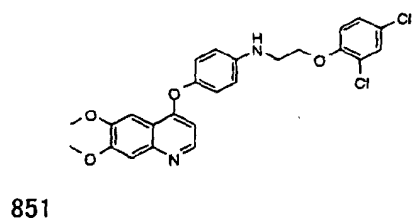
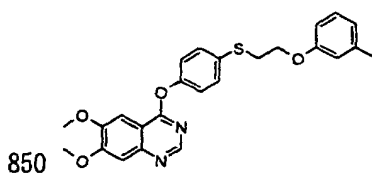
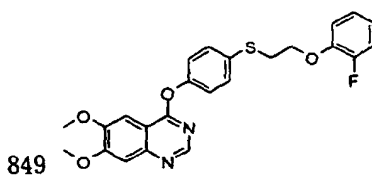
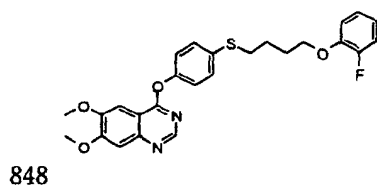
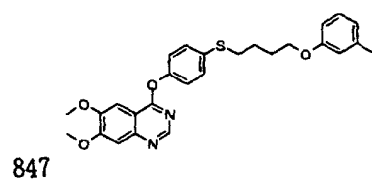


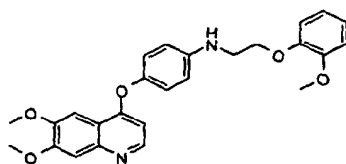
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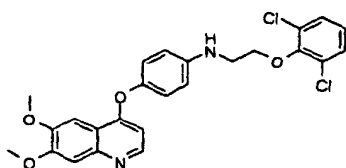
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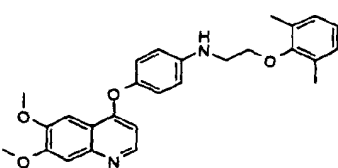




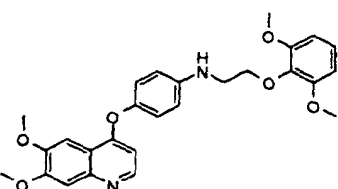
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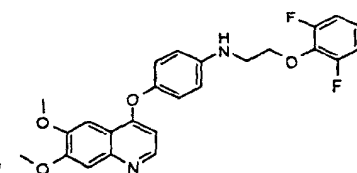
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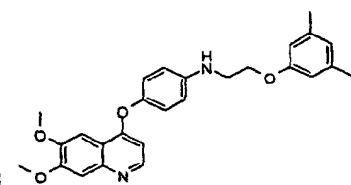
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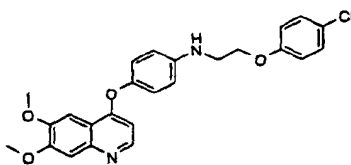


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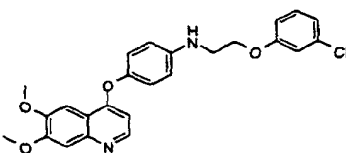


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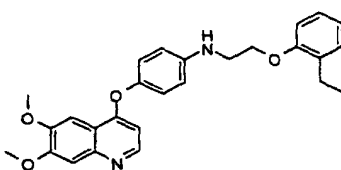
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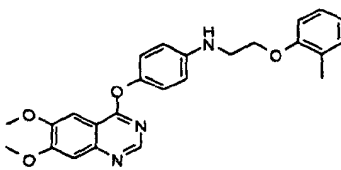
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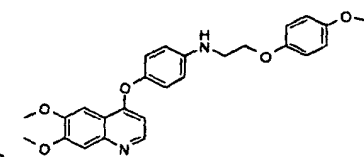
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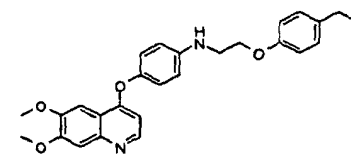
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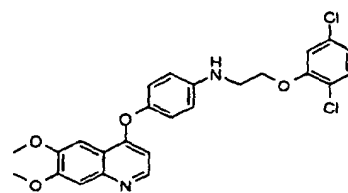
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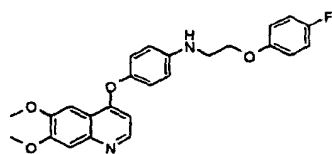


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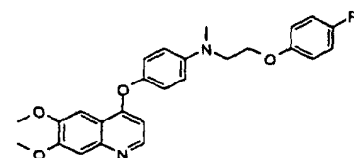
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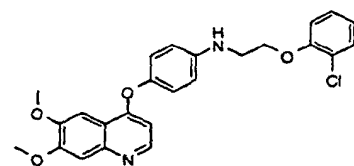
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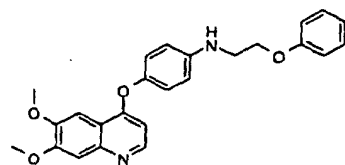
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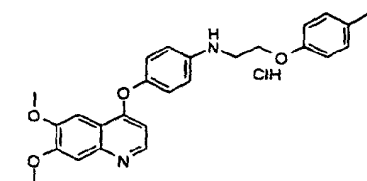
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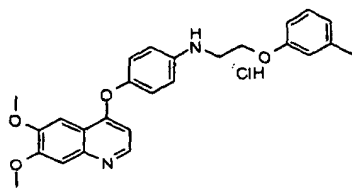
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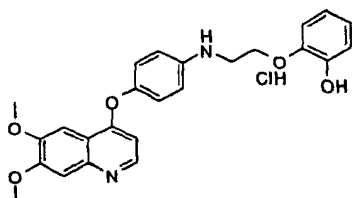


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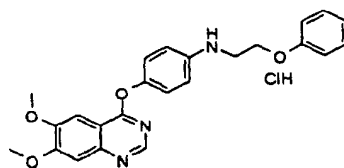
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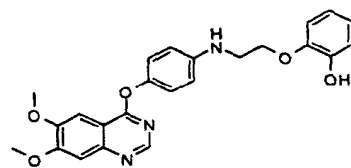
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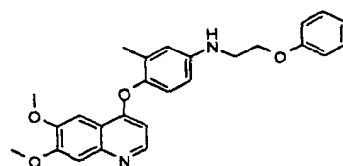
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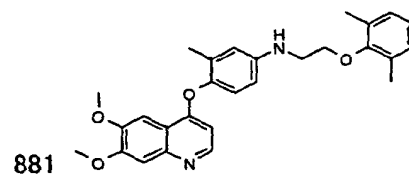
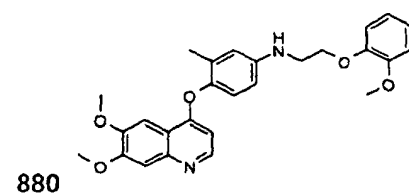
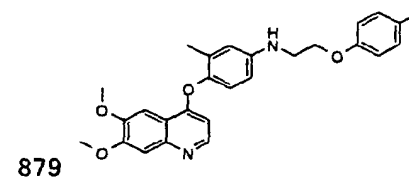
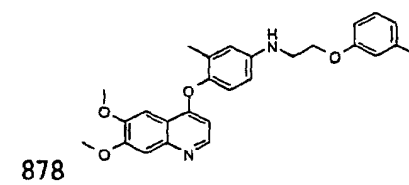
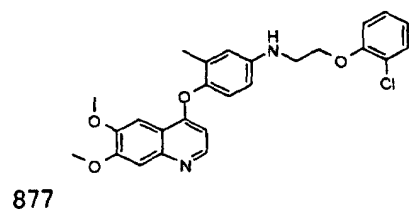
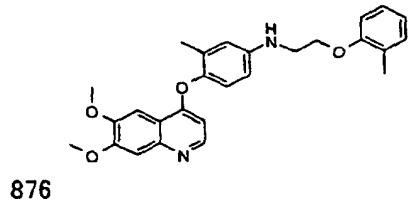
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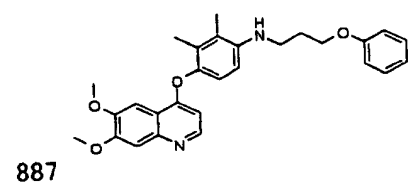
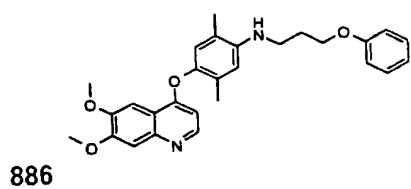
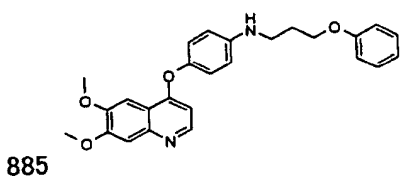
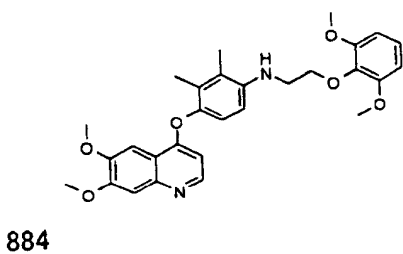
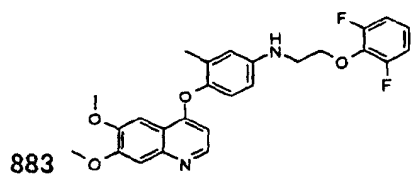
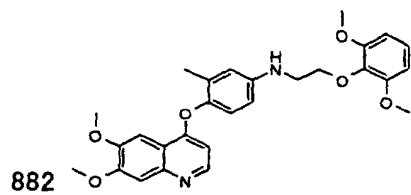


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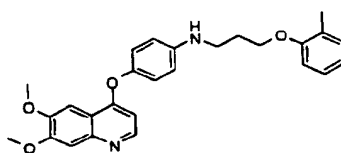


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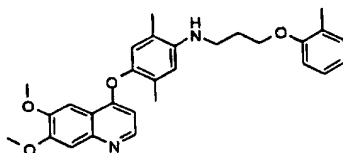




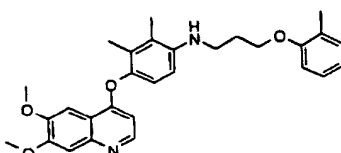
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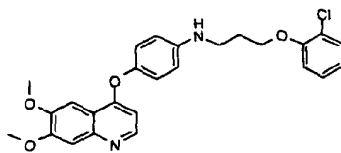
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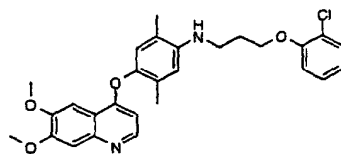
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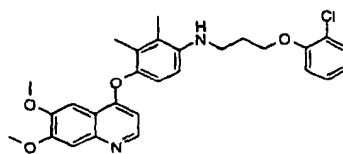
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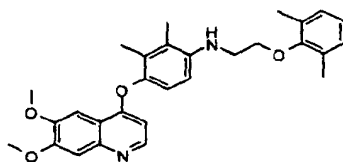
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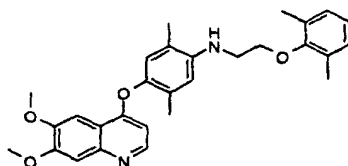
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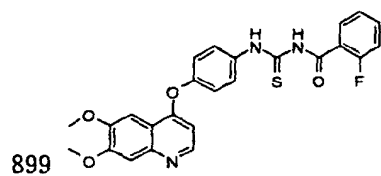
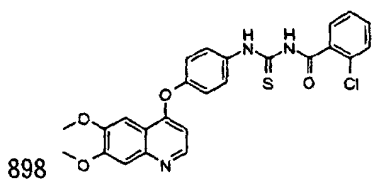
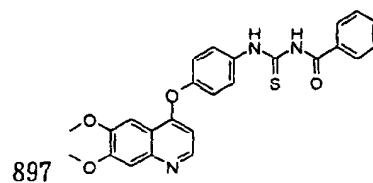
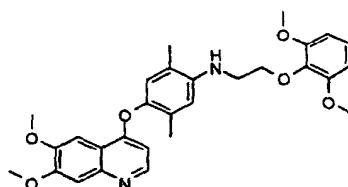
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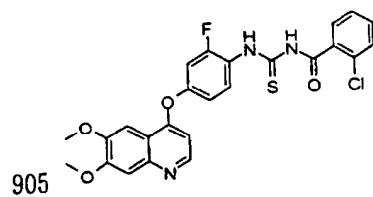
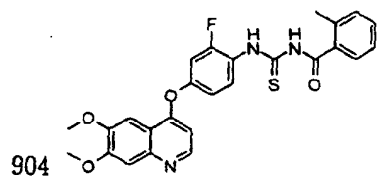
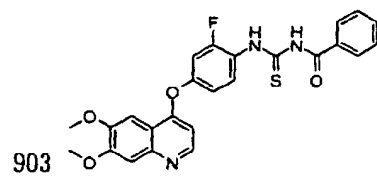
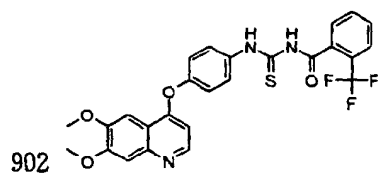
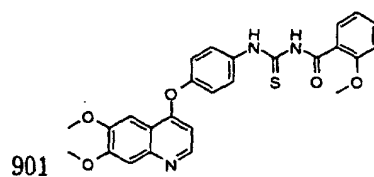
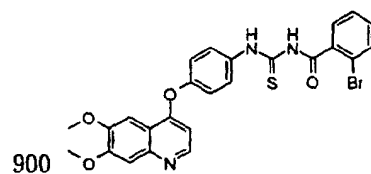


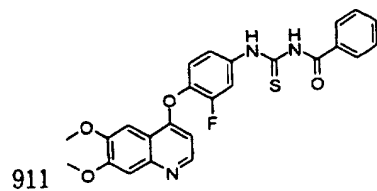
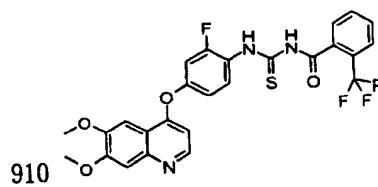
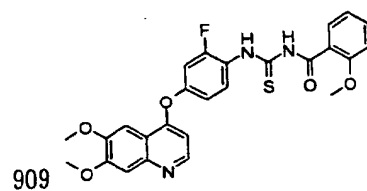
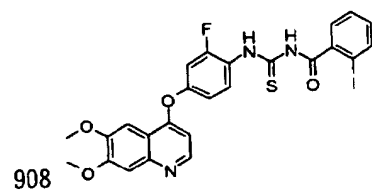
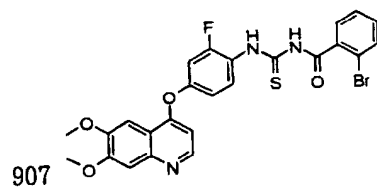
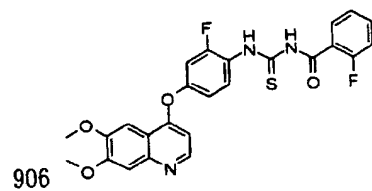
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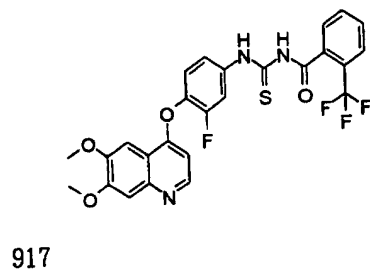
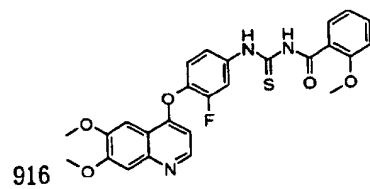
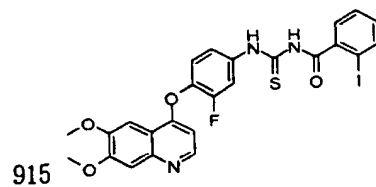
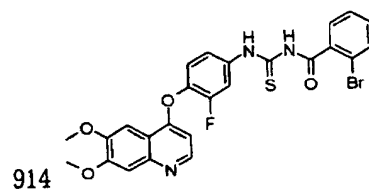
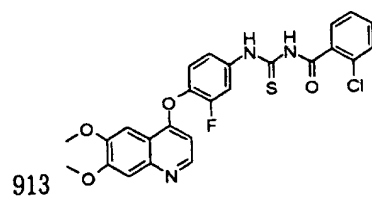
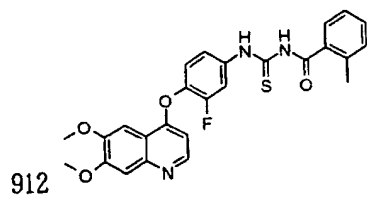


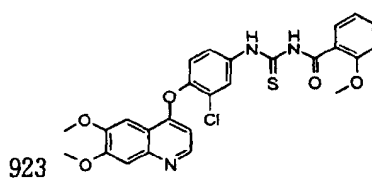
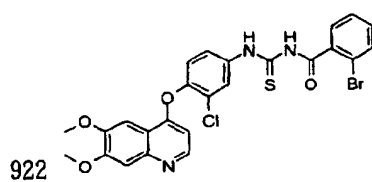
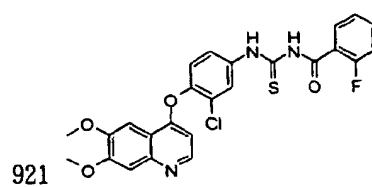
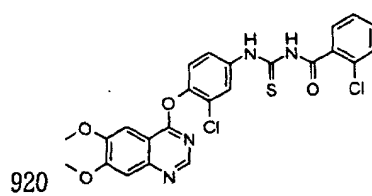
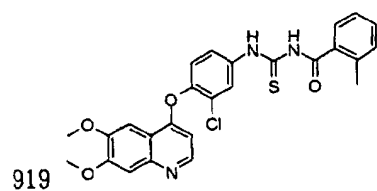
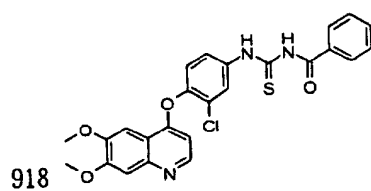
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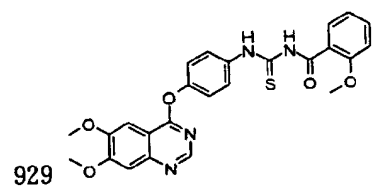
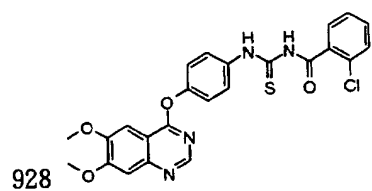
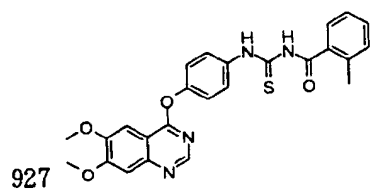
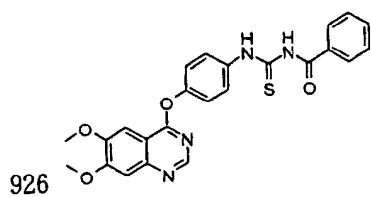
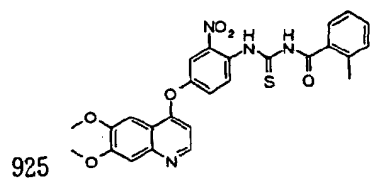
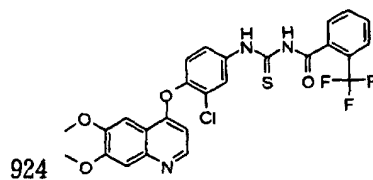


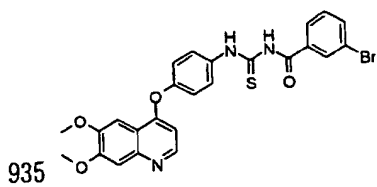
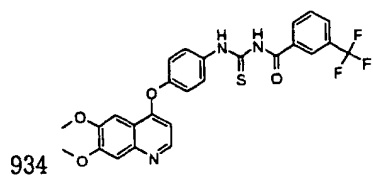
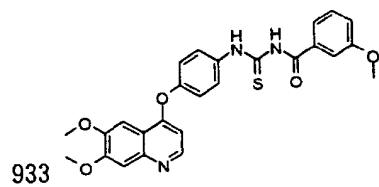
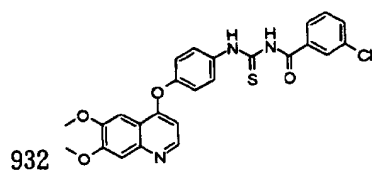
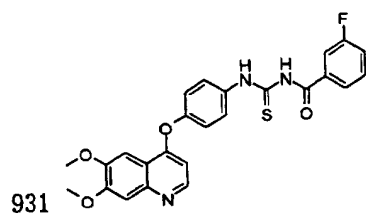
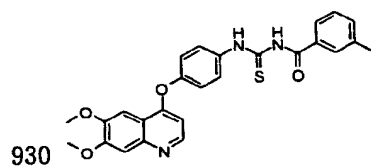


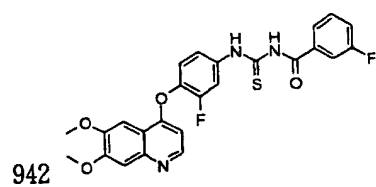
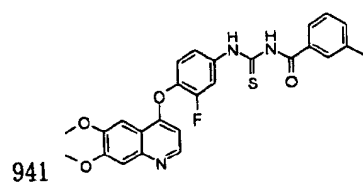
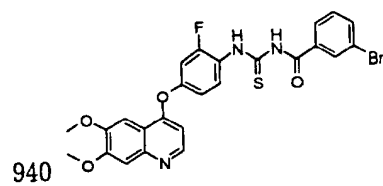
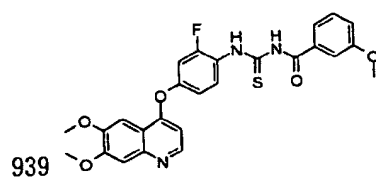
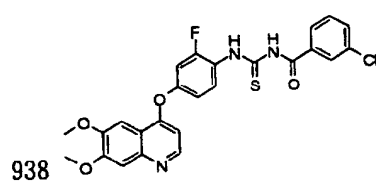
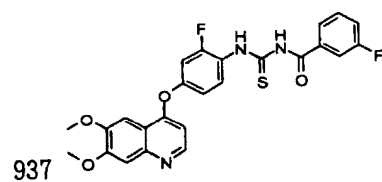
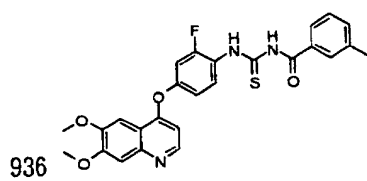


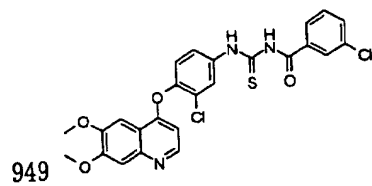
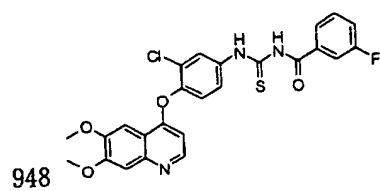
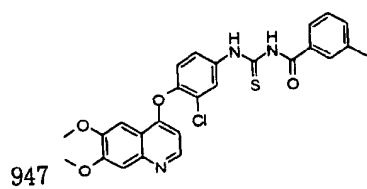
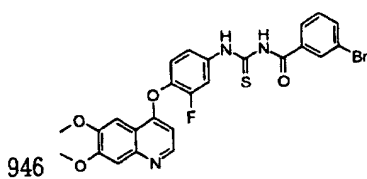
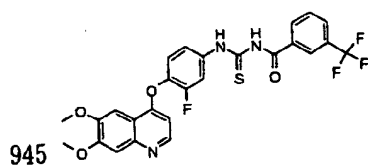
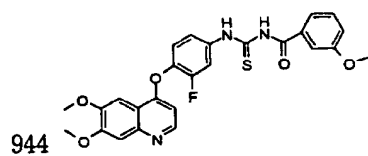
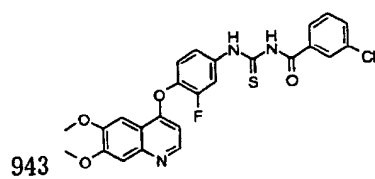


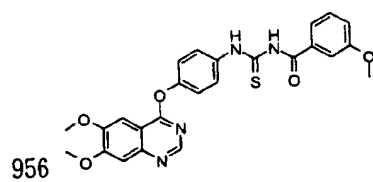
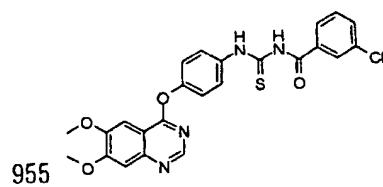
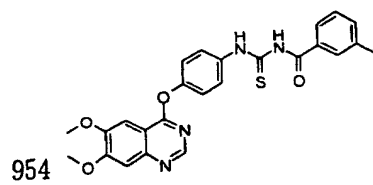
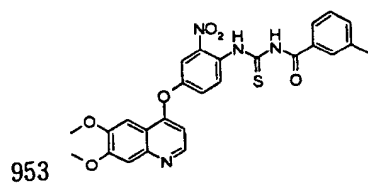
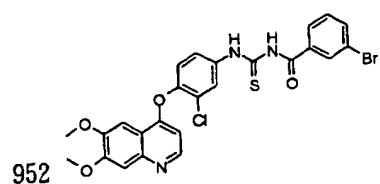
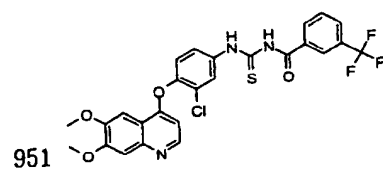
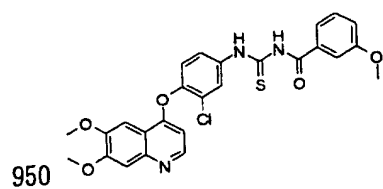


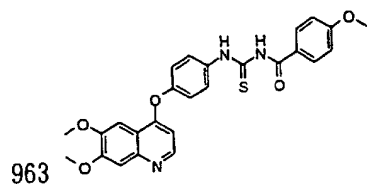
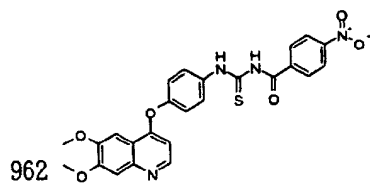
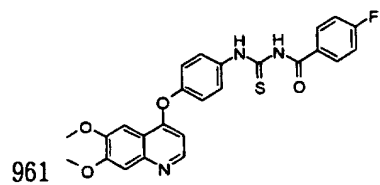
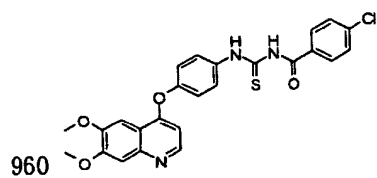
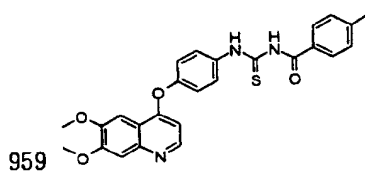
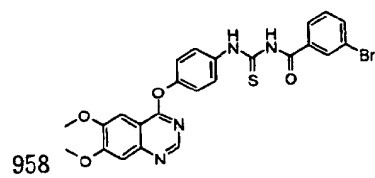
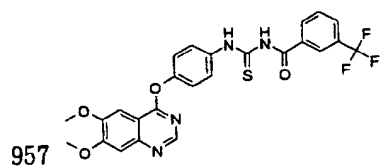


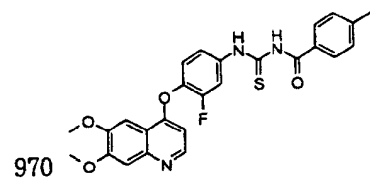
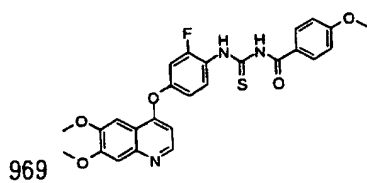
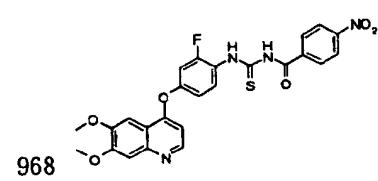
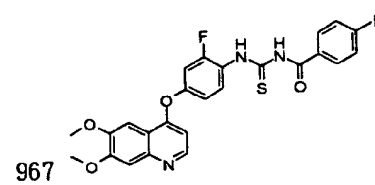
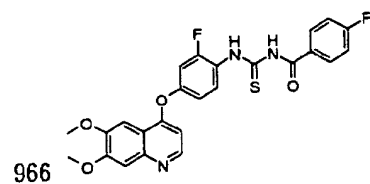
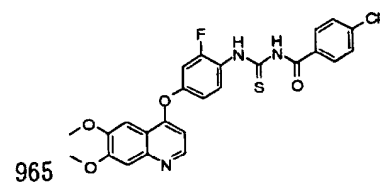
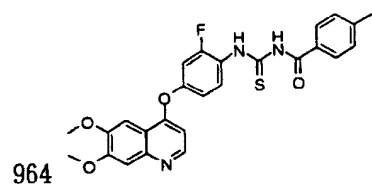


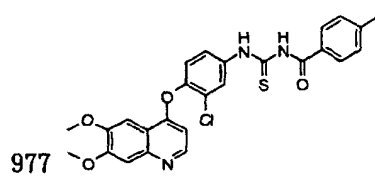
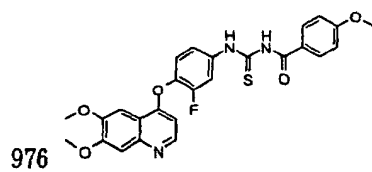
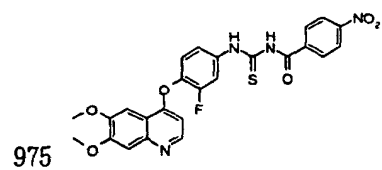
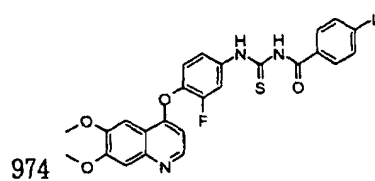
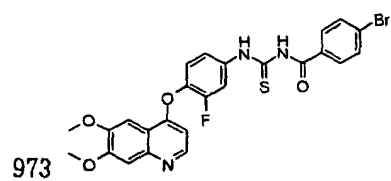
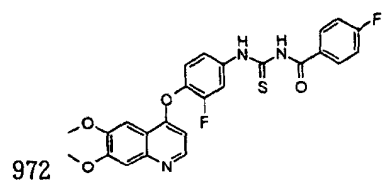
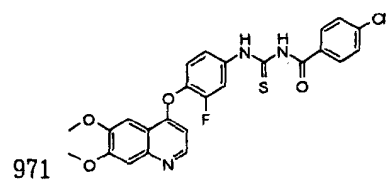


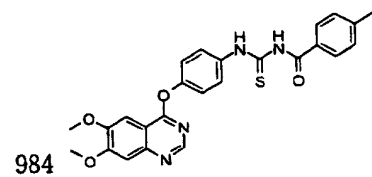
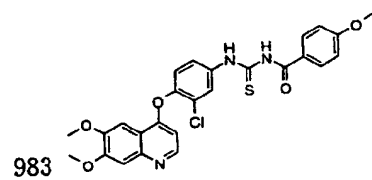
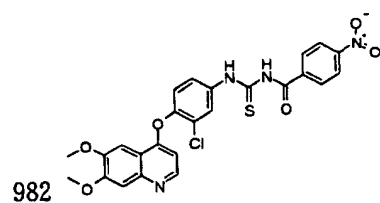
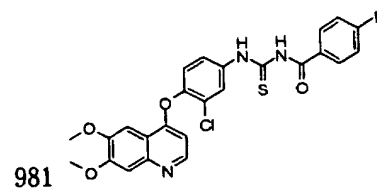
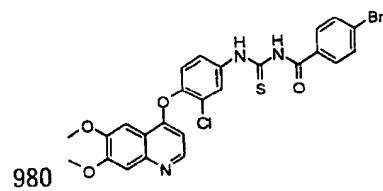
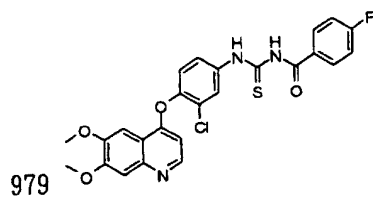
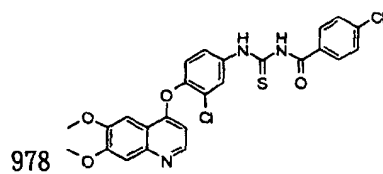


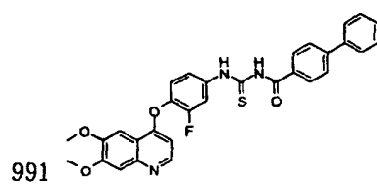
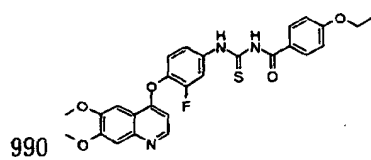
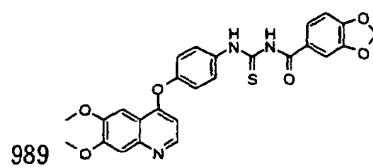
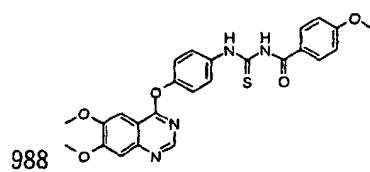
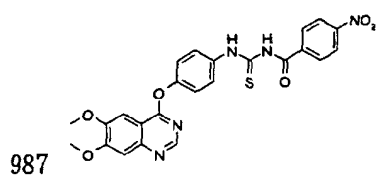
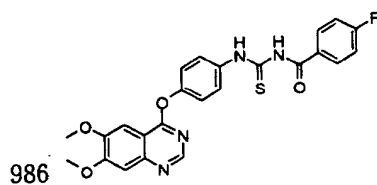
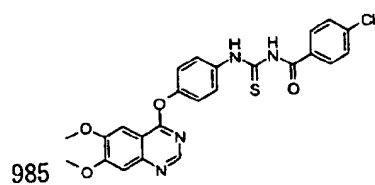


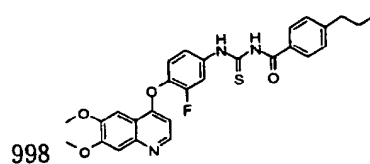
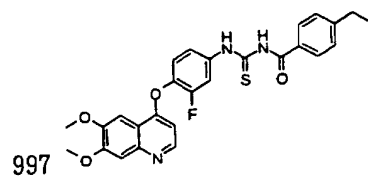
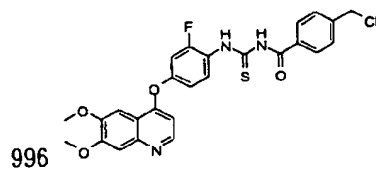
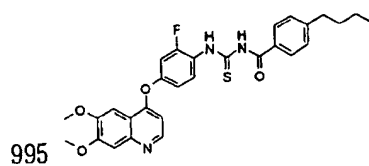
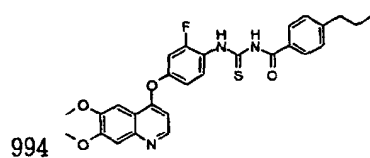
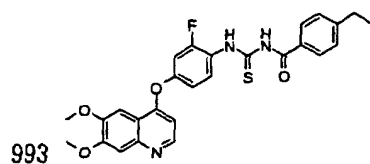
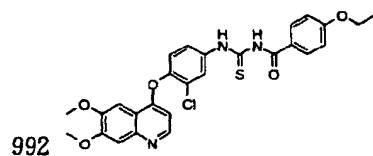




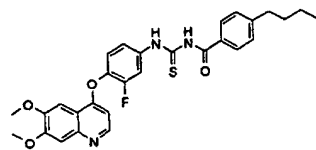




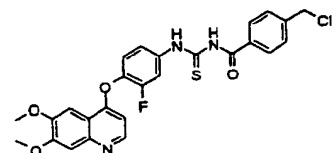




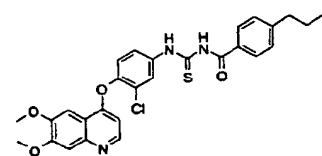
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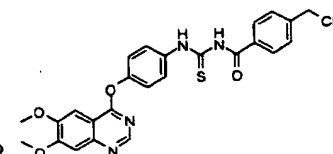
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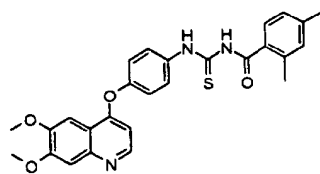
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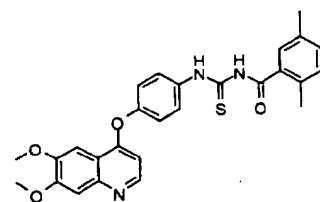
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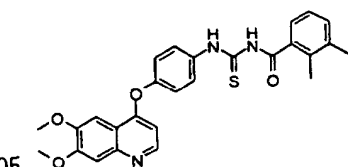
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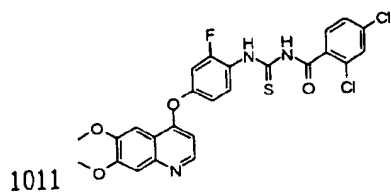
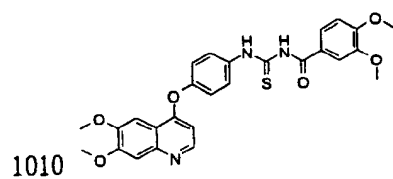
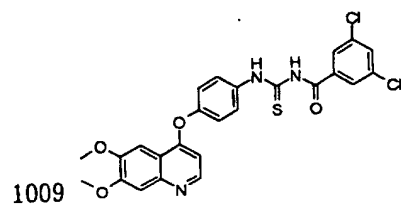
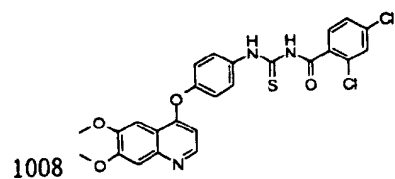
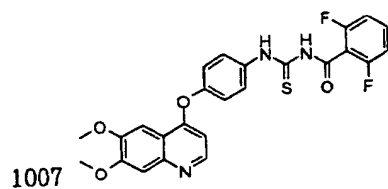
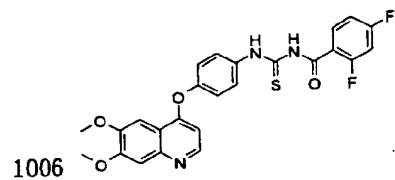


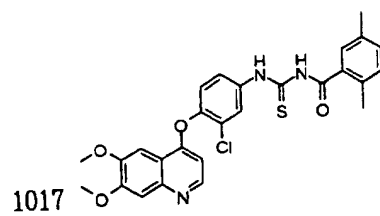
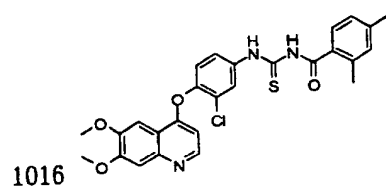
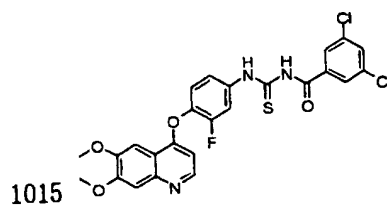
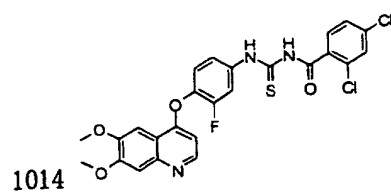
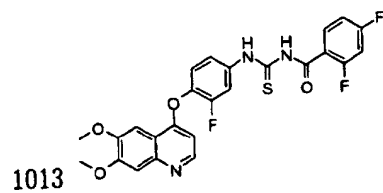
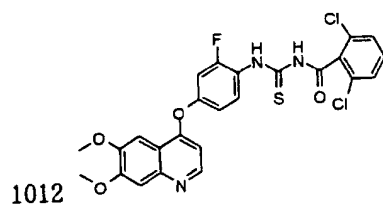
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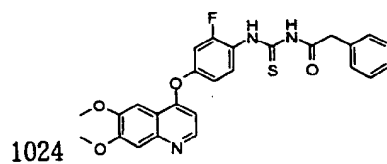
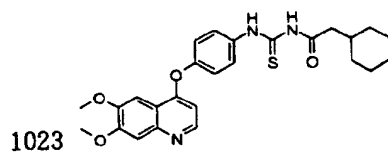
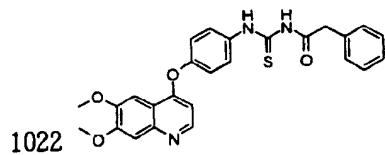
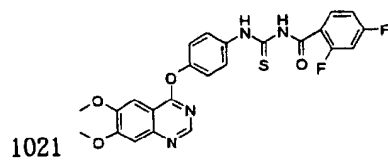
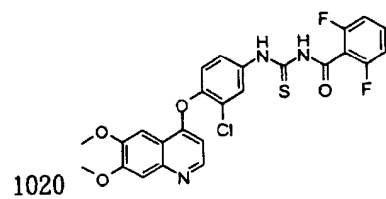
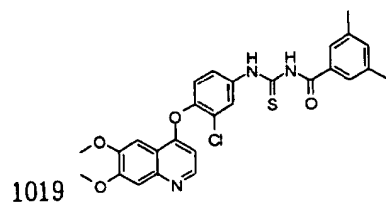
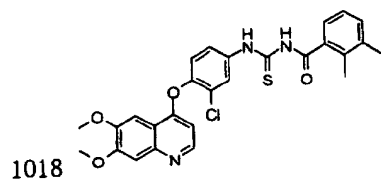


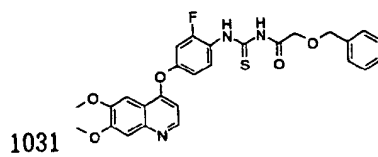
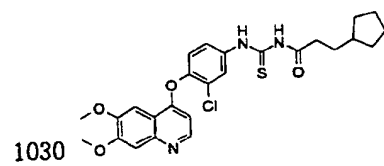
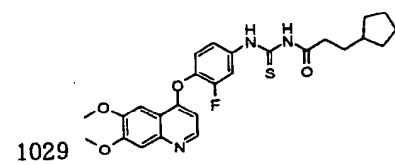
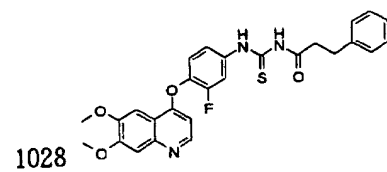
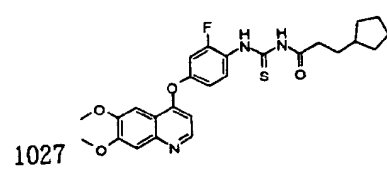
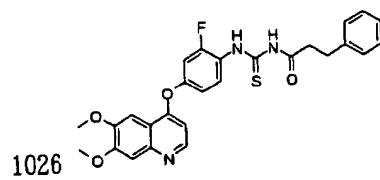
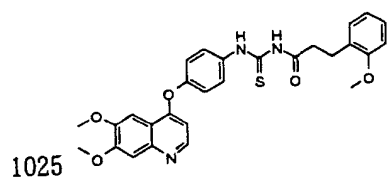
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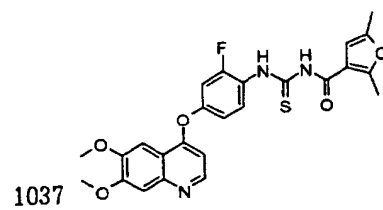
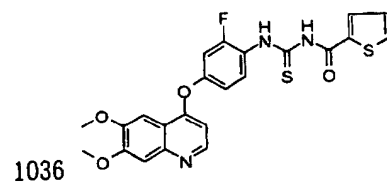
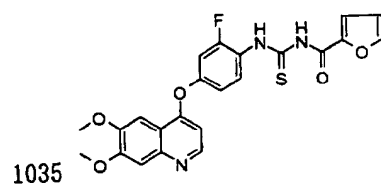
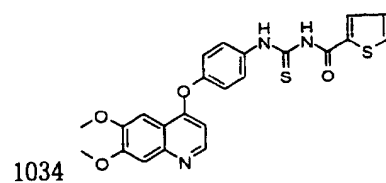
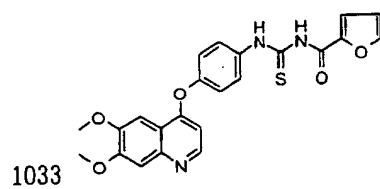
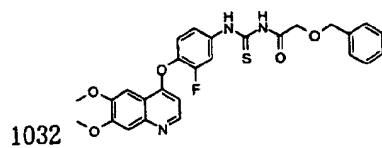


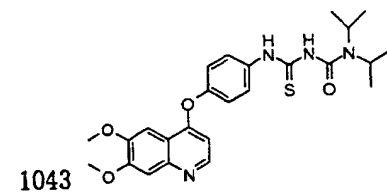
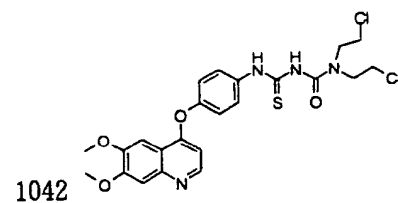
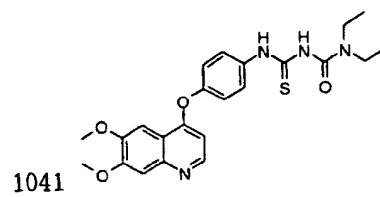
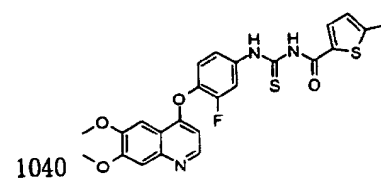
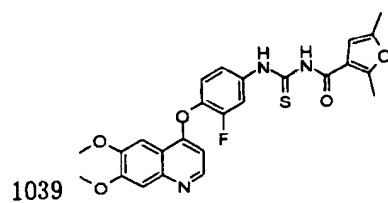
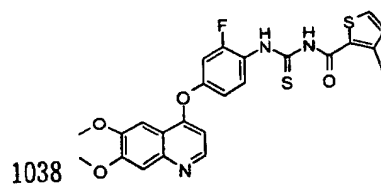


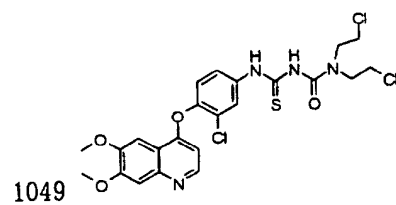
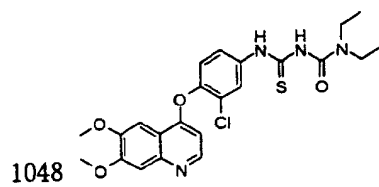
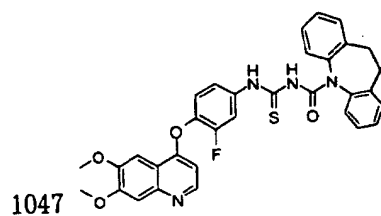
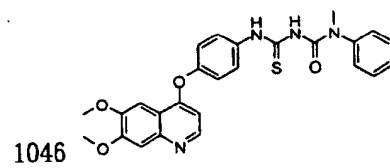
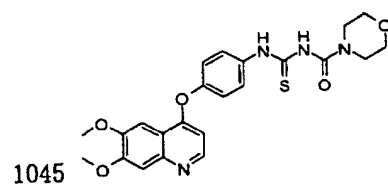
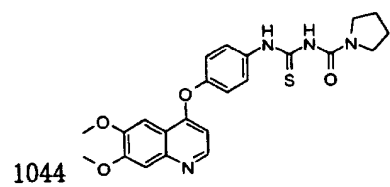


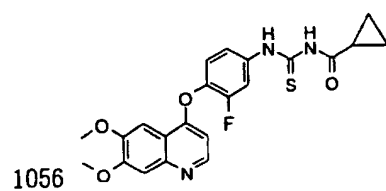
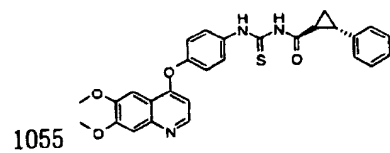
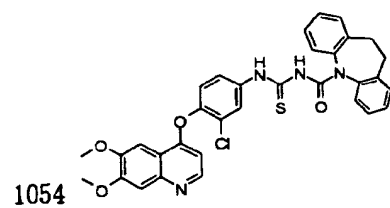
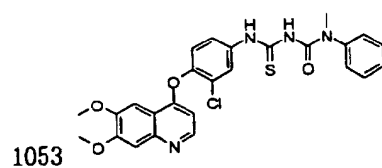
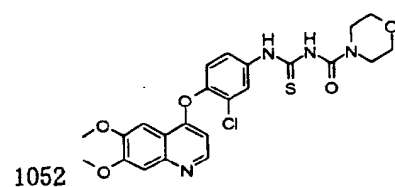
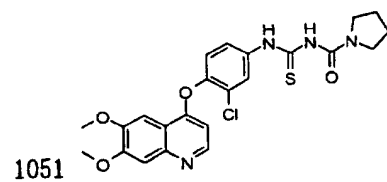
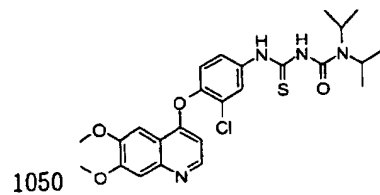


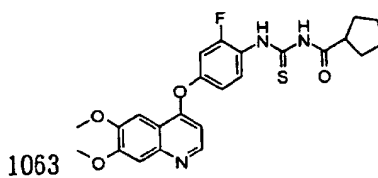
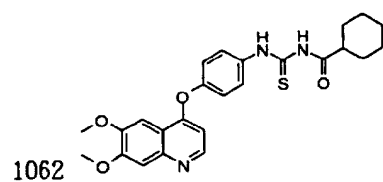
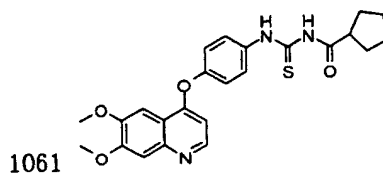
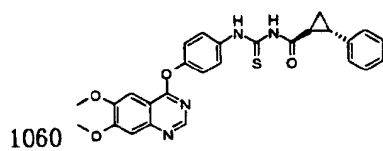
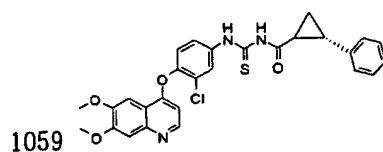
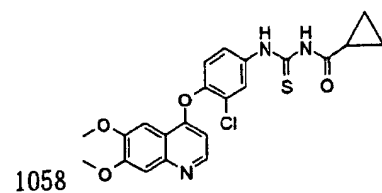
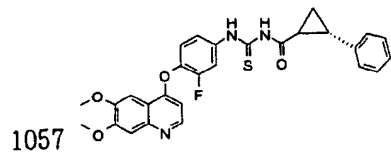


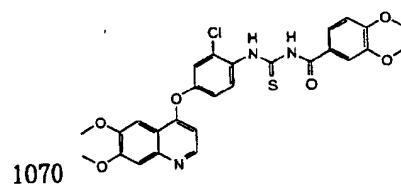
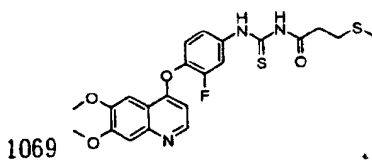
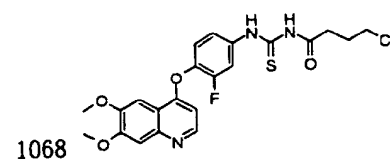
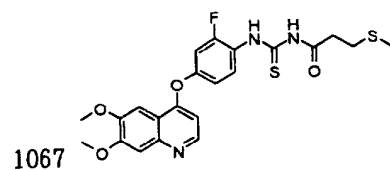
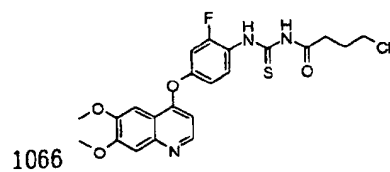
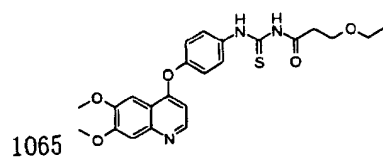
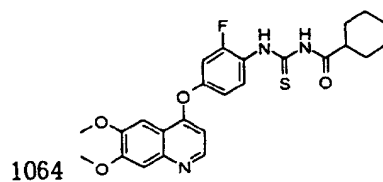


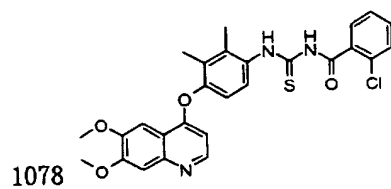
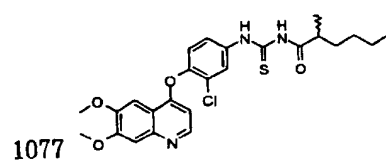
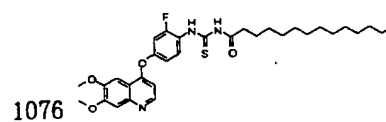
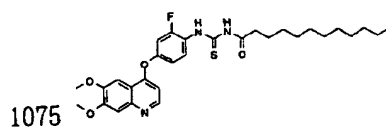
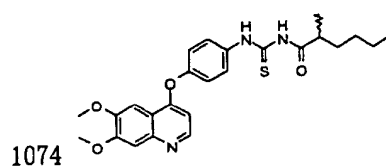
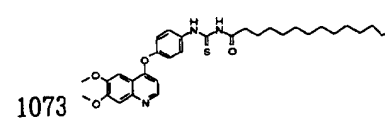
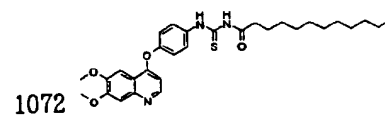
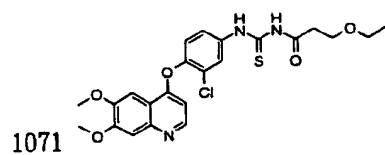


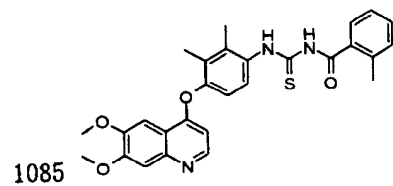
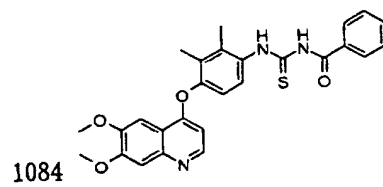
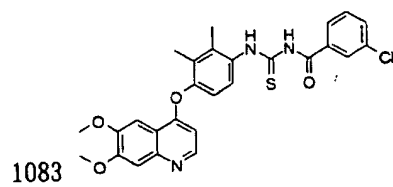
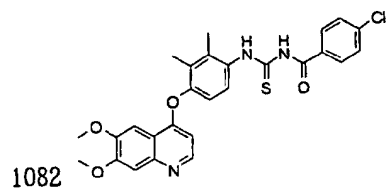
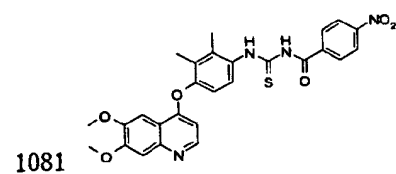
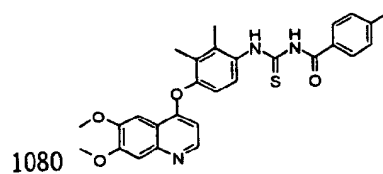
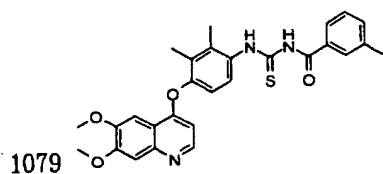


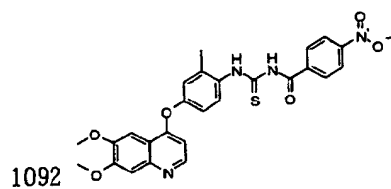
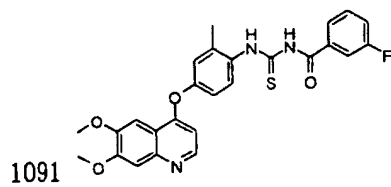
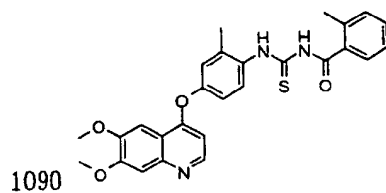
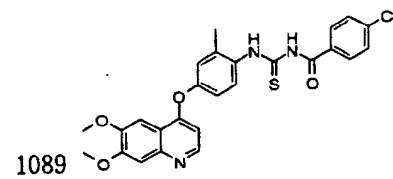
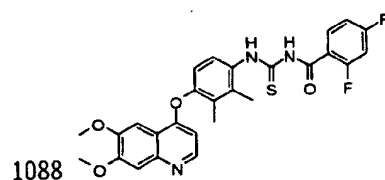
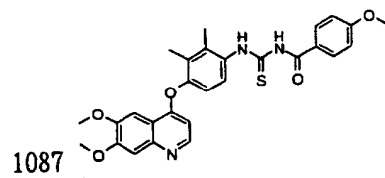
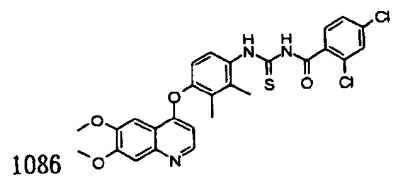


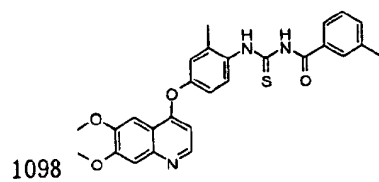
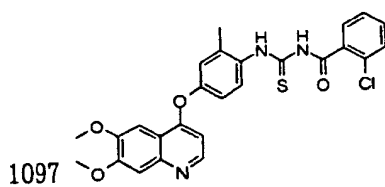
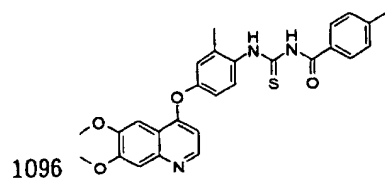
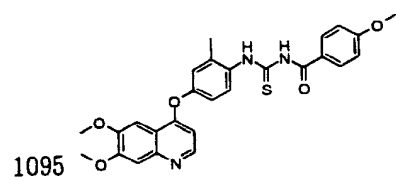
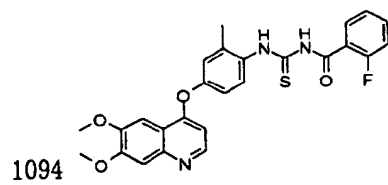
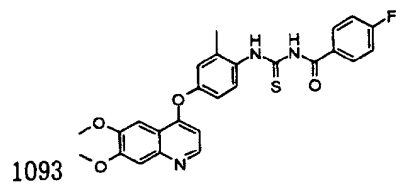


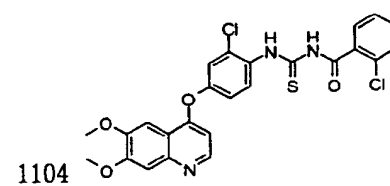
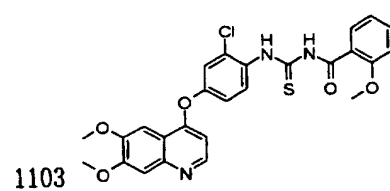
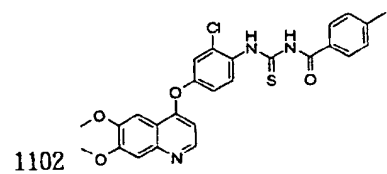
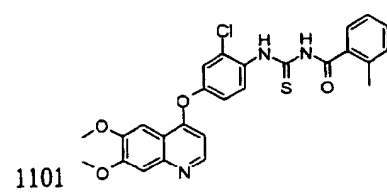
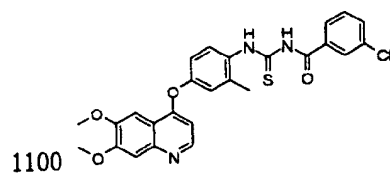
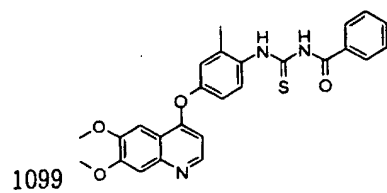


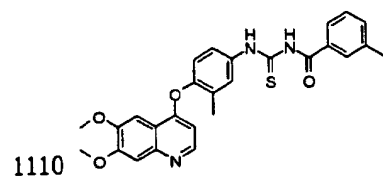
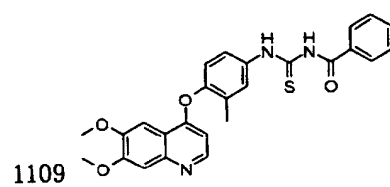
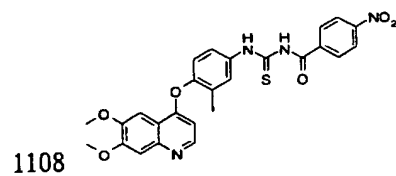
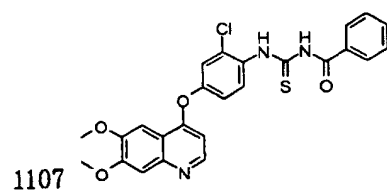
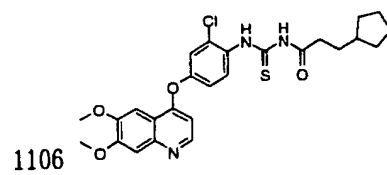
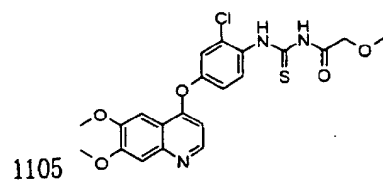






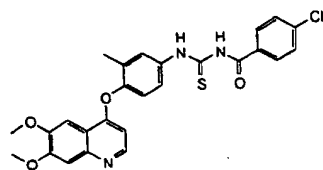






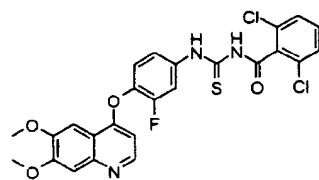
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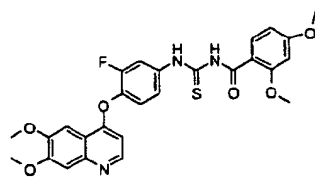
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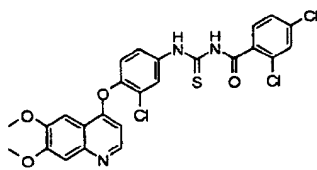
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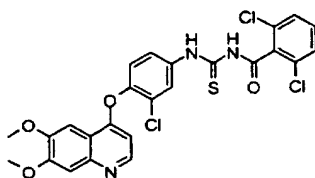
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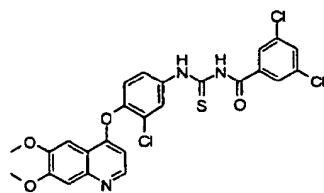
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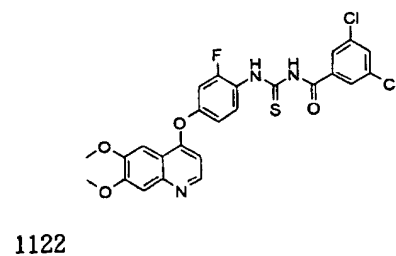
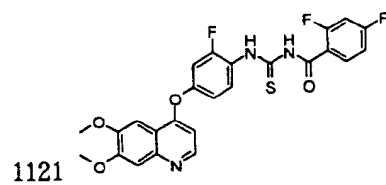
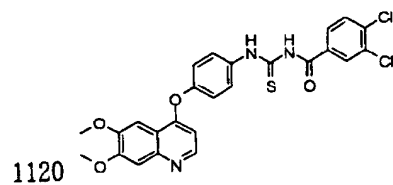
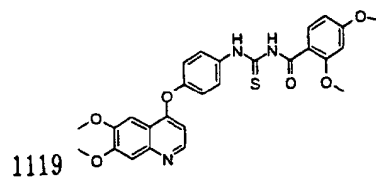
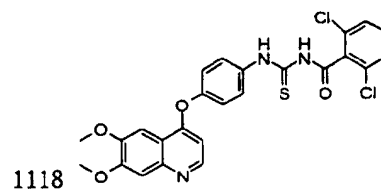
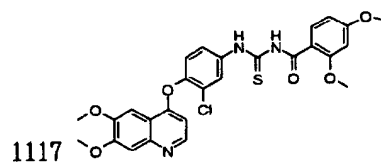
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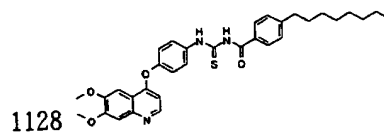
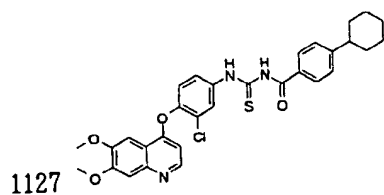
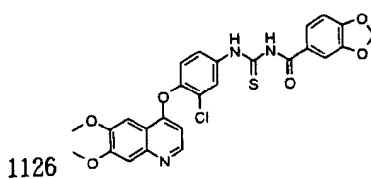
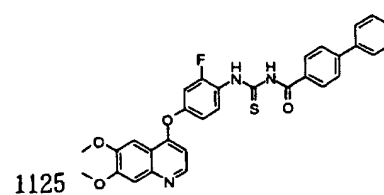
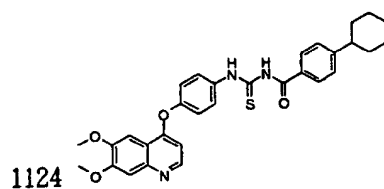
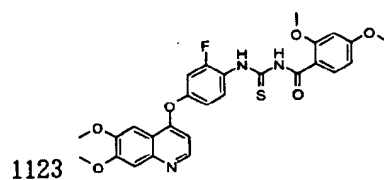
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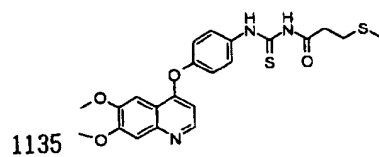
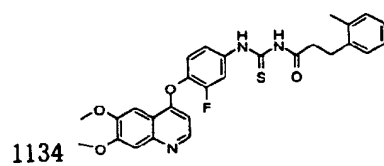
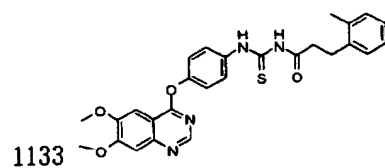
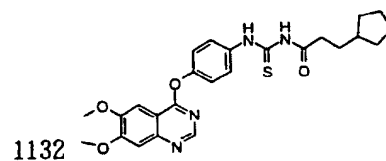
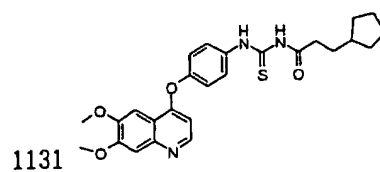
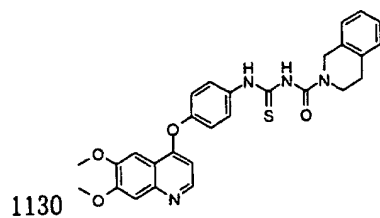
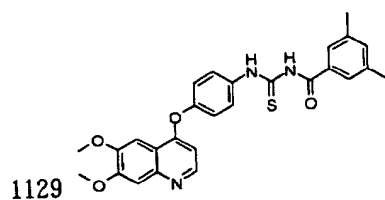
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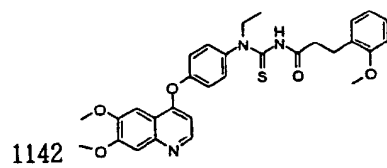
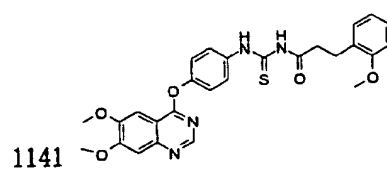
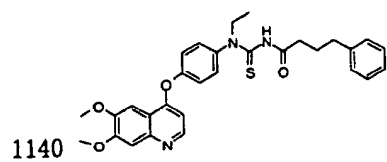
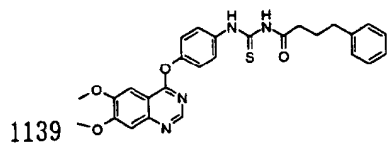
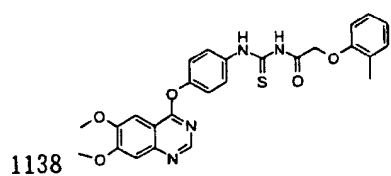
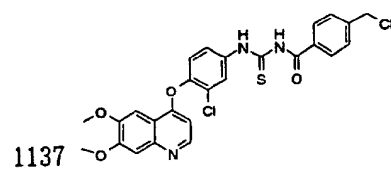
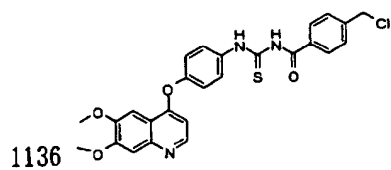


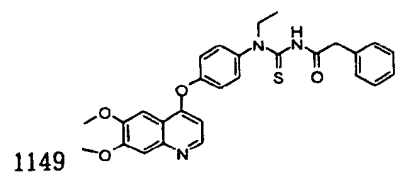
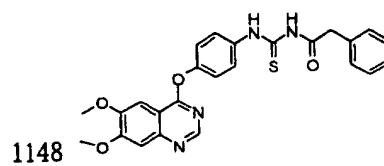
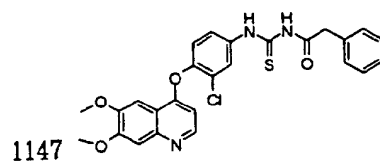
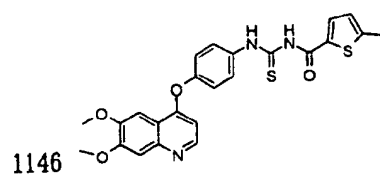
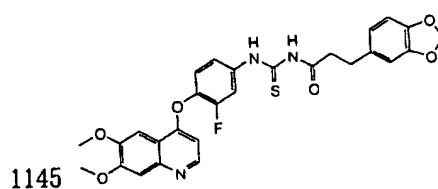
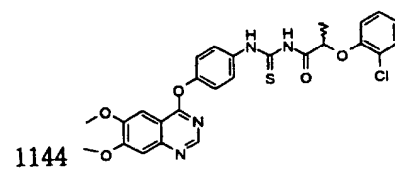
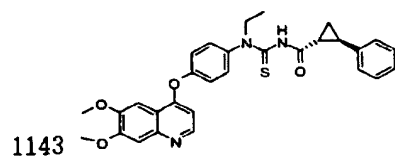
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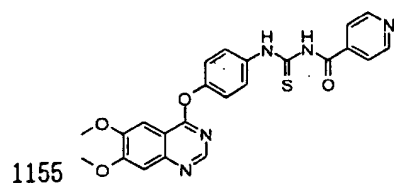
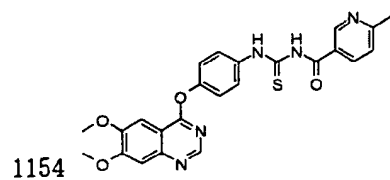
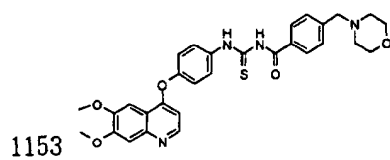
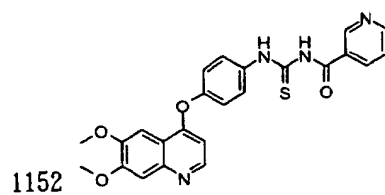
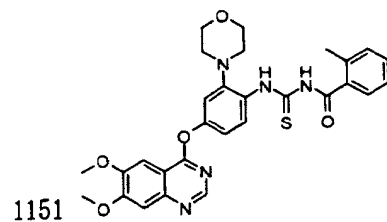
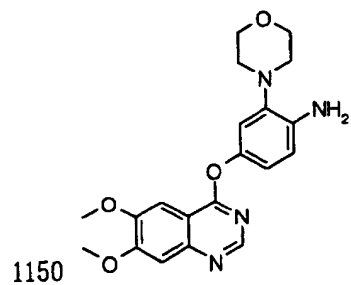


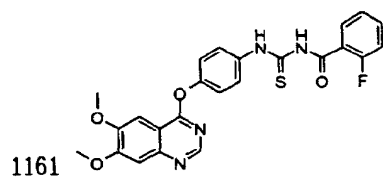
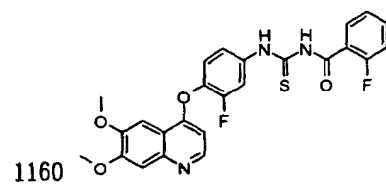
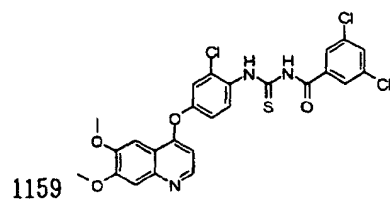
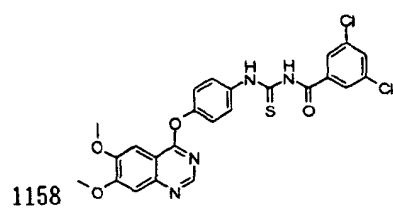
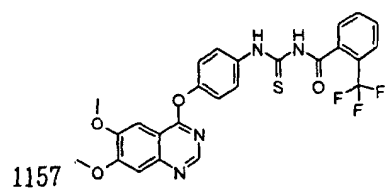
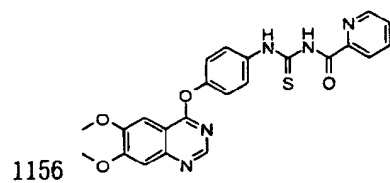


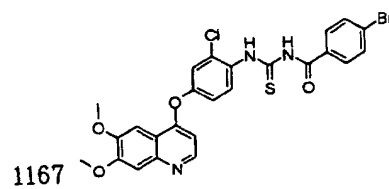
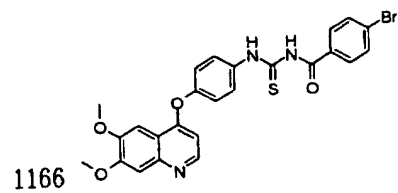
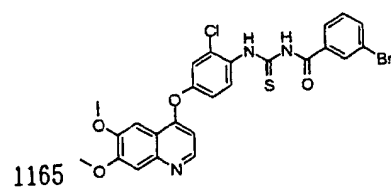
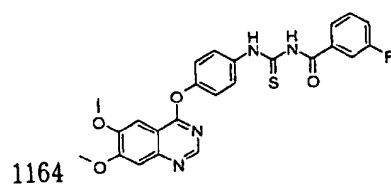
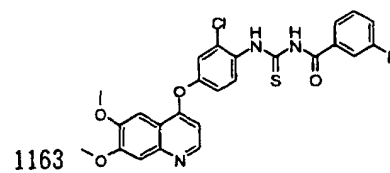
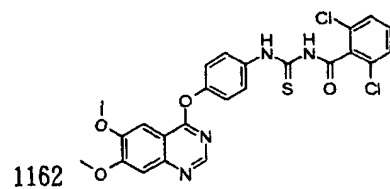


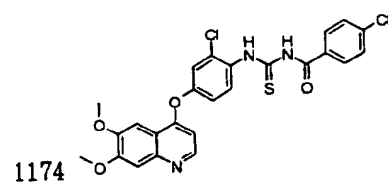
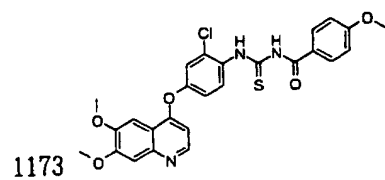
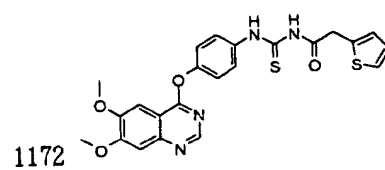
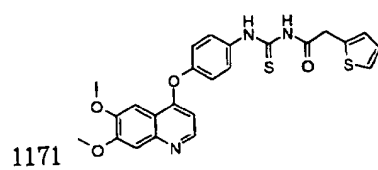
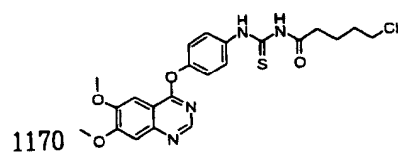
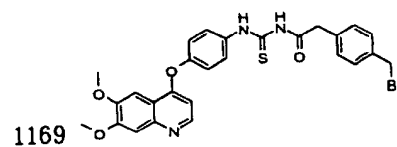
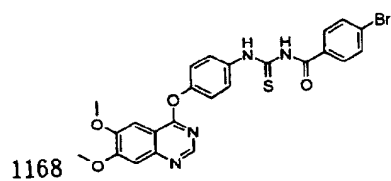


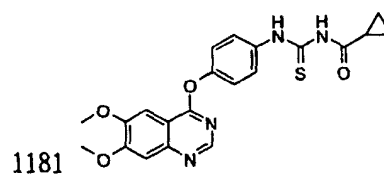
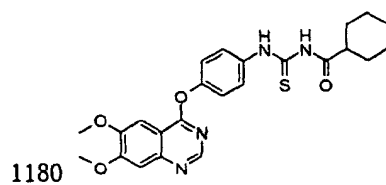
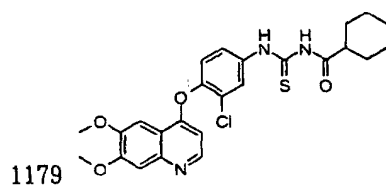
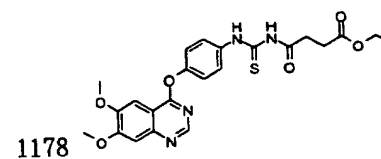
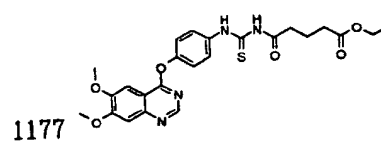
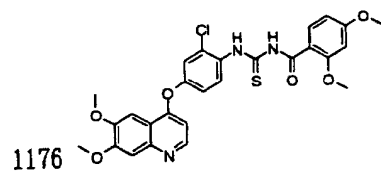
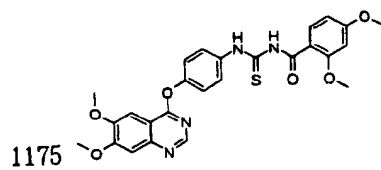


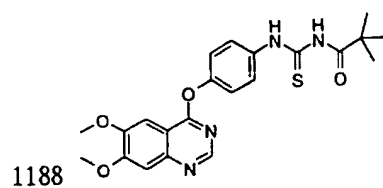
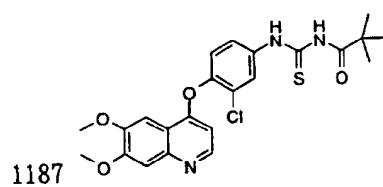
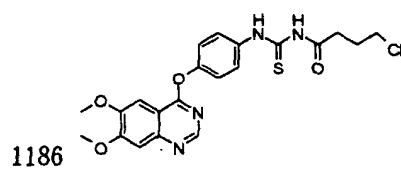
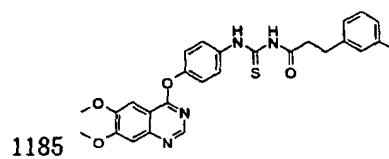
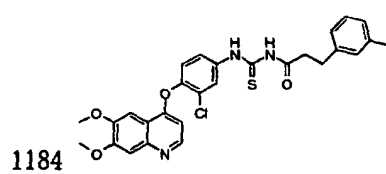
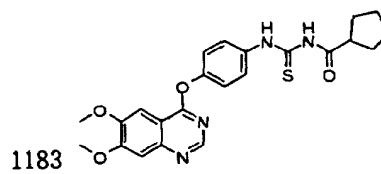
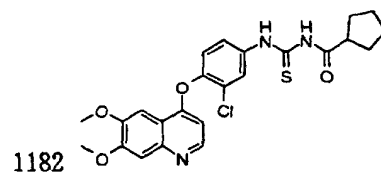


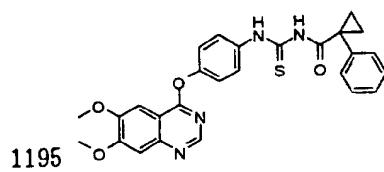
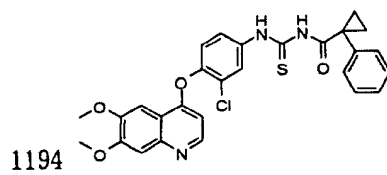
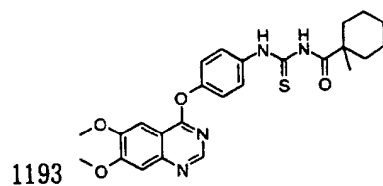
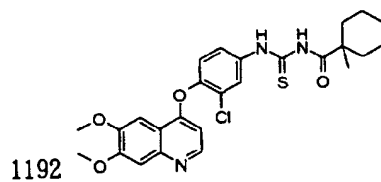
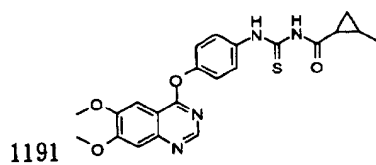
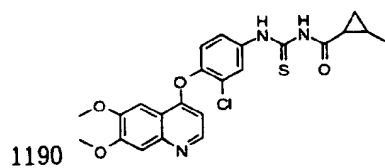
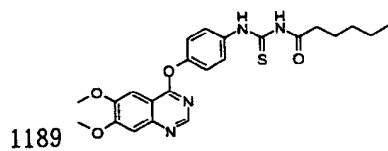






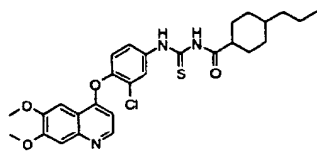






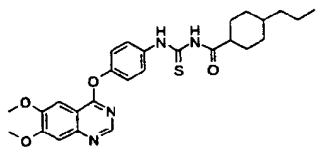
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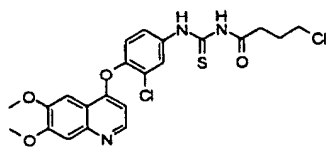
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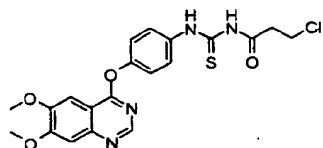
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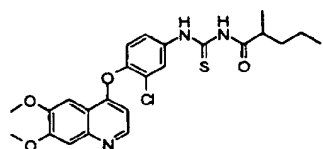
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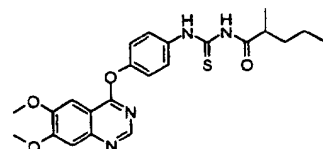
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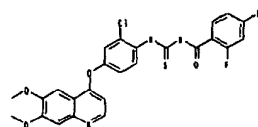
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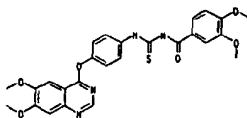
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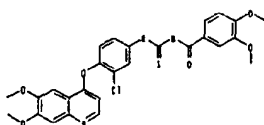


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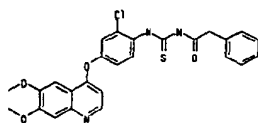
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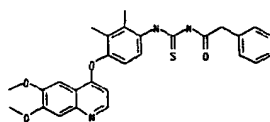
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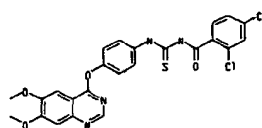
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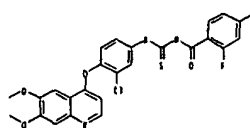
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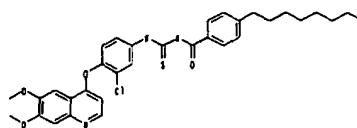
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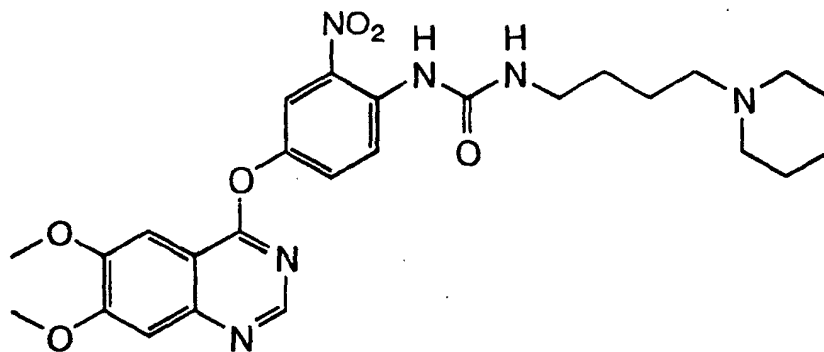
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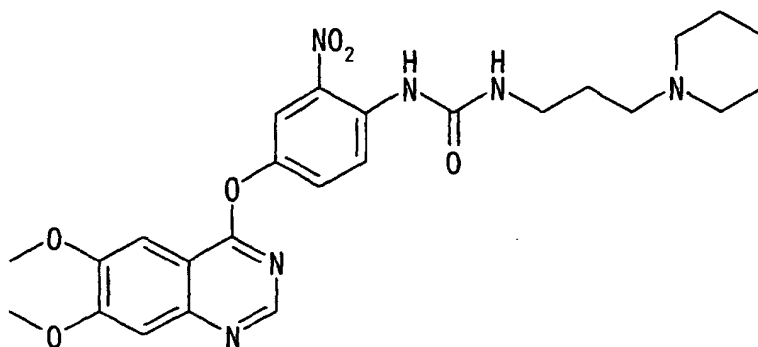
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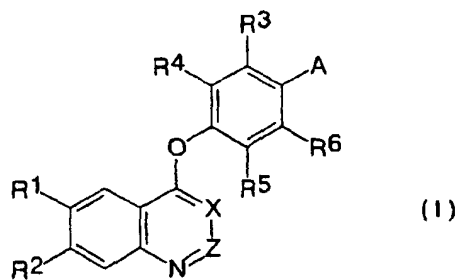


1 2 1 1



Claims

1. A compound represented by formula (I) or a pharmacologically acceptable salt or solvate thereof:



wherein

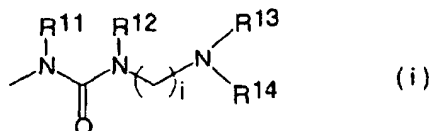
X and Z, which may be the same or different, represent CH or N;

R¹ and R², which may be the same or different, represent a hydrogen atom or C₁₋₄ alkoxy optionally substituted by a halogen atom;

R³, R⁴, R⁵, and R⁶, which may be the same or different, represent a hydrogen atom; a halogen atom; C₁₋₄ alkyl optionally substituted by a halogen atom; C₁₋₄ alkoxy optionally substituted by a halogen atom; nitro; amino; or morpholyl;

A represents a group selected from the group consisting of formulae (i) to (x), wherein R¹¹ and R¹², which may be the same or different, represent a hydrogen atom, C₁₋₄ alkyl optionally substituted by a halogen atom, or C₁₋₄ alkylcarbonyl optionally substituted by a halogen atom;

provided that compounds wherein R³, R⁴, R⁵ and R⁶ represent a hydrogen atom and A represents group (v) wherein u is 0 (zero) and R¹⁹ represents phenyl optionally substituted by a halogen atom, C₁₋₄ alkyl, or C₁₋₄ alkoxy are excluded:

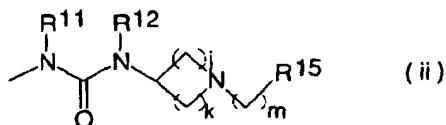


wherein

i is an integer of 0 to 10,

R¹³ and R¹⁴, which may be the same or different, represent a hydrogen atom; C₁₋₆ alkyl optionally substituted by a halogen atom; or phenyl optionally substituted by a halogen atom or C₁₋₄ alkyl optionally substituted by a halogen atom,

R¹³ and R¹⁴ may form a five- to seven-membered saturated or unsaturated heterocyclic ring optionally containing one or more additional hetero-atoms together with the nitrogen atom to which they are attached, and this heterocyclic ring is optionally substituted by a halogen atom or C₁₋₄ alkyl optionally substituted by a halogen atom, or, R¹³ or R¹⁴ may form C₁₋₄ alkylene optionally substituted by a halogen atom together with R¹²;



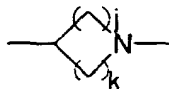
wherein

j is an integer of 0 to 3,

k is an integer of 0 to 3, provided that both j and k are not 0 (zero),

m is an integer of 0 to 2,

carbon atoms in the following



are optionally substituted by one or more C₁₋₄ alkyl groups, which may be the same or different, optionally substituted by a halogen atom, and

R¹⁵ represents a hydrogen atom; cyclic C₃₋₇ alkyl optionally substituted by a halogen atom; phenyl optionally substituted by C₁₋₆ alkyl or a halogen atom; or C₁₋₄ alkoxy carbonyl;



n is 0 (zero) or 1.

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q is 0 (zero) or 1.

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u is 0 (zero) or 1,

545

(1) phenyl which is optionally substituted by C₁₋₁₀ alkyl optionally substituted by a halogen atom; C₁₋₁₀ alkoxy optionally substituted by a halogen atom; -NR³¹R³² wherein R³¹ and R³², which may be the same or different, represent a hydrogen atom or C₁₋₄ alkyl optionally substituted by a halogen atom; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(2) phenoxy of which the phenyl portion is optionally substituted by C₁₋₁₀ alkyl optionally substituted by a halogen atom; C₁₋₁₀ alkoxy optionally substituted by a halogen atom; -NR³¹R³² wherein R³¹ and R³² are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(3) cyclic C₃₋₇ alkyl which is optionally condensed with another carbocyclic ring or heterocyclic ring to form an eight- to twelve-membered bicyclic saturated or unsaturated carbocyclic ring or heterocyclic ring and the carbocyclic ring and the heterocyclic ring are optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom; phenyl optionally substituted by a halogen atom; cyclic C₃₋₇ alkyl optionally substituted by a halogen atom; or a halogen atom,

(4) a five- to seven-membered saturated or unsaturated heterocyclic ring which is optionally condensed with another carbocyclic or heterocyclic ring to form a ten- to twelve-membered bicyclic saturated or unsaturated heterocyclic ring optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom, or a halogen atom,

(5) C₁₋₁₆ alkyl,

(6) C₂₋₆ alkenyl, or

(7) C₂₋₆ alkynyl,

wherein (5) C₁₋₁₆ alkyl, (6) C₂₋₆ alkenyl, and (7) C₂₋₆ alkynyl are optionally substituted by one or more of the following groups:

(a) phenyl optionally substituted by C₁₋₁₀ alkyl optionally substituted by a halogen atom; C₁₋₁₀ alkoxy optionally substituted by a halogen atom; -NR³¹R³² wherein R³¹ and R³² are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(b) phenoxy of which the phenyl portion is optionally substituted by C₁₋₁₀ alkyl optionally substituted by a halogen atom; C₁₋₁₀ alkoxy optionally substituted by a halogen atom; -NR³¹R³² wherein R³¹ and R³² are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(c) phenylthio of which the phenyl portion is optionally substituted by C₁₋₁₀ alkyl optionally substituted by a halogen atom; C₁₋₁₀ alkoxy optionally substituted by a halogen atom; -NR³¹R³² wherein R³¹ and R³² are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(d) -NR³³R³⁴ wherein R³³ and R³⁴ are as defined in R¹³ and R¹⁴,

(e) cyclic C₃₋₇ alkyl which is optionally condensed with another carbocyclic ring or heterocyclic ring to form an eight- to twelve-membered bicyclic saturated or unsaturated carbocyclic ring or heterocyclic ring and the carbocyclic ring and the heterocyclic ring are optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom; phenyl optionally substituted by a halogen atom; or a halogen atom,

(f) a five- to seven-membered saturated or unsaturated heterocyclic ring which is optionally condensed with another carbocyclic ring or heterocyclic ring to form a ten- to twelve-membered bicyclic saturated or unsaturated heterocyclic ring optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom, or a halogen atom,

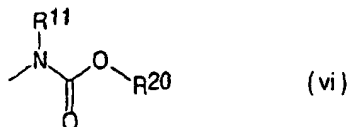
(g) naphthyl,

(h) cyano,

(i) C₁₋₄ alkylthio optionally substituted by a halogen atom,

(j) a halogen atom, or

(k) alkoxycarbonyl optionally substituted by a halogen atom;



wherein
R²⁰ represents

(1) phenyl optionally substituted by C₁₋₆ alkyl optionally substituted by a halogen atom; C₁₋₆ alkoxy optionally

substituted by a halogen atom; $-NR^{35}R^{36}$ wherein R^{35} and R^{36} , which may be the same or different, represent a hydrogen atom or C_{1-4} alkyl optionally substituted by a halogen atom; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(2) cyclic C_{3-7} alkyl which is optionally condensed with another carbocyclic ring or heterocyclic ring to form an eight- to twelve-membered bicyclic saturated or unsaturated carbocyclic ring or heterocyclic ring and the carbocyclic ring and the heterocyclic ring are optionally substituted by C_{1-4} alkyl optionally substituted by a halogen atom, or a halogen atom,

(3) a five- to seven-membered saturated or unsaturated heterocyclic ring which is optionally condensed with another carbocyclic ring or heterocyclic ring to form a ten- to twelve-membered bicyclic saturated or unsaturated heterocyclic ring optionally substituted by C_{1-4} alkyl optionally substituted by a halogen atom, or a halogen atom,

(4) C_{1-20} alkyl,

(5) C_{2-6} alkenyl, or

(6) C_{2-6} alkynyl, and

wherein (4) C_{1-20} alkyl, (5) C_{2-6} alkenyl, and (6) C_{2-6} alkynyl are optionally substituted by one or more of the following groups:

(a) phenyl optionally substituted by C_{1-6} alkyl optionally substituted by a halogen atom; C_{1-6} alkoxy optionally substituted by a halogen atom; $-NR^{35}R^{36}$ wherein R^{35} and R^{36} are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(b) phenoxy of which the phenyl portion is optionally substituted by C_{1-6} alkyl optionally substituted by a halogen atom; C_{1-6} alkoxy optionally substituted by a halogen atom; $-NR^{35}R^{36}$ wherein R^{35} and R^{36} are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(c) phenylthio of which the phenyl portion is optionally substituted by C_{1-6} alkyl optionally substituted by a halogen atom; C_{1-6} alkoxy optionally substituted by a halogen atom; $-NR^{35}R^{36}$ wherein R^{35} and R^{36} are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

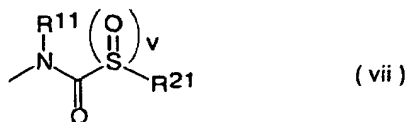
(d) $-NR^{37}R^{38}$ wherein R^{37} and R^{38} are as defined in R^{13} and R^{14} ,

(e) cyclic C_{3-7} alkyl which is optionally condensed with another carbocyclic ring or heterocyclic ring to form an eight- to twelve-membered bicyclic saturated or unsaturated carbocyclic ring or heterocyclic ring and the carbocyclic ring and the heterocyclic ring are optionally substituted by C_{1-4} alkyl optionally substituted by a halogen atom, or a halogen atom,

(f) a five- to seven-membered saturated or unsaturated heterocyclic ring which is optionally condensed with another carbocyclic ring or heterocyclic ring to form a ten- to twelve-membered bicyclic saturated or unsaturated heterocyclic ring optionally substituted by C_{1-4} alkyl optionally substituted by a halogen atom, or a halogen atom,

(g) naphthyl, or

(h) cyano;



wherein

v is an integer of 0 to 2,

R^{21} represents

(1) phenyl optionally substituted by C_{1-6} alkyl optionally substituted by a halogen atom; C_{1-6} alkoxy optionally substituted by a halogen atom; $-NR^{39}R^{40}$ wherein R^{39} and R^{40} , which may be the same or different, represent a hydrogen atom or C_{1-4} alkyl optionally substituted by a halogen atom; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(2) cyclic C_{3-7} alkyl which is optionally condensed with another carbocyclic ring or heterocyclic ring to form an eight- to twelve-membered bicyclic saturated or unsaturated carbocyclic ring or heterocyclic ring and the carbocyclic ring and the heterocyclic ring are optionally substituted by C_{1-4} alkyl optionally substituted by a halogen atom, or a halogen atom,

(3) a five- to seven-membered saturated or unsaturated heterocyclic ring which is optionally condensed with another carbocyclic ring or heterocyclic ring to form a ten- to twelve-membered bicyclic saturated or unsaturated heterocyclic ring optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom, or a halogen atom,

(4) C₁₋₂₀ alkyl,

(5) C₂₋₆ alkenyl, or

(6) C₂₋₆ alkynyl, and

wherein (4) C₁₋₂₀ alkyl, (5) C₂₋₆ alkenyl, and (6) C₂₋₆ alkynyl are optionally substituted by one or more of the following groups:

(a) phenyl optionally substituted by C₁₋₆ alkyl optionally substituted by a halogen atom; C₁₋₆ alkoxy optionally substituted by a halogen atom; -NR³⁹R⁴⁰ wherein R³⁹ and R⁴⁰ are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(b) phenoxy of which the phenyl portion is optionally substituted by C₁₋₆ alkyl optionally substituted by a halogen atom; C₁₋₆ alkoxy optionally substituted by a halogen atom; -NR³⁹R⁴⁰ wherein R³⁹ and R⁴⁰ are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

(c) phenylthio of which the phenyl portion is optionally substituted by C₁₋₆ alkyl optionally substituted by a halogen atom; C₁₋₆ alkoxy optionally substituted by a halogen atom; -NR³⁹R⁴⁰ wherein R³⁹ and R⁴⁰ are as defined above; phenyl optionally substituted by a halogen atom; a halogen atom; or cyano,

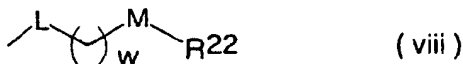
(d) -NR⁴¹R⁴² wherein R⁴¹ and R⁴² are as defined in R¹³ and R¹⁴,

(e) cyclic C₃₋₇ alkyl which is optionally condensed with another carbocyclic ring or heterocyclic ring to form an eight- to twelve-membered bicyclic saturated or unsaturated carbocyclic ring or heterocyclic ring and the carbocyclic ring and the heterocyclic ring are optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom, or a halogen atom,

(f) a five- to seven-membered saturated or unsaturated heterocyclic ring which is optionally condensed with another carbocyclic ring or heterocyclic ring to form a ten- to twelve-membered bicyclic saturated or unsaturated heterocyclic ring optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom, or a halogen atom,

(g) naphthyl, or

(h) cyano;



wherein

w is an integer of 1 to 4,

L represents -O-, -S(=O)y-, wherein y is an integer of 0 to 2, or -N(-R¹¹)-,

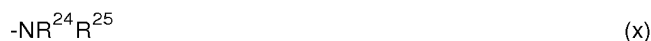
M represents -O-, -C(=O)-O-, -S(=O)z-, wherein z is an integer of 0 to 2, -N(-R¹²)-, -C(=O)-N(-R¹²)-, or -C(=O)-,

R²² represents a hydrogen atom; C₁₋₄ alkyl optionally substituted by a halogen atom; or phenyl optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom, C₁₋₄ alkoxy optionally substituted by a halogen atom, nitro, amino, or a halogen atom,

when M represents -N(-R¹²)- or -C(=O)-N(-R¹²)-, R²² and R¹² may form a five- to seven-membered saturated or unsaturated heterocyclic ring optionally containing one or more additional hetero-atoms together with the nitrogen atom to which they are attached, this heterocyclic ring is optionally condensed with another carbocyclic ring or heterocyclic ring to form a ten- to twelve-membered bicyclic saturated or unsaturated heterocyclic ring, and these heterocyclic rings are optionally substituted by C₁₋₄ alkyl optionally substituted by a halogen atom; phenyl; benzyl; or piperidine;



wherein R²³ represents a hydrogen atom or C₁₋₄ alkyl optionally substituted by a halogen atom; and



wherein R^{24} and R^{25} , which may be the same or different, represent a hydrogen atom or C_{1-4} alkyl optionally substituted by a halogen atom.

2. The compound according to claim 1, wherein X represents CH or N and Z represents CH.
3. The compound according to claim 1, wherein R^1 and R^2 represent C_{1-4} alkoxy and at least one of R^3 , R^4 , R^5 , and R^6 represents a group other than a hydrogen atom.
4. The compound according to claim 1, wherein R^1 and R^2 represent C_{1-4} alkoxy, R^3 represents a group other than a hydrogen atom, and R^4 , R^5 , and R^6 represent a hydrogen atom.
5. The compound according to claim 1, wherein R^1 and R^2 represent C_{1-4} alkoxy and A represents group (i) wherein i is an integer of 1 to 3; and R^{13} and R^{14} , which may be the same or different, represent C_{1-4} alkyl, or may form a five- to seven-membered saturated heterocyclic ring optionally substituted by C_{1-4} alkyl together with the nitrogen atom to which they are attached.
6. The compound according to claim 1, wherein R^1 and R^2 represent C_{1-4} alkoxy, R^3 , R^4 , R^5 , and R^6 represent a hydrogen atom, and A represents group (i) wherein i is an integer of 1 to 3 and R^{13} and R^{14} , which may be the same or different, represent C_{1-4} alkyl, or may form a five- to seven-membered saturated heterocyclic ring optionally substituted by C_{1-4} alkyl together with the nitrogen atom to which they are attached.
7. The compound according to claim 1, wherein R^1 and R^2 represent C_{1-4} alkoxy, R^3 represents a group other than a hydrogen atom, R^4 , R^5 , and R^6 represent a hydrogen atom, and A represents group (i) wherein i is an integer of 1 to 3 and R^{13} and R^{14} , which may be the same or different, represent C_{1-4} alkyl, or may form a five- to seven-membered saturated heterocyclic ring optionally substituted by C_{1-4} alkyl together with the nitrogen atom to which they are attached.
8. The compound according to claim 1, wherein R^1 and R^2 represent C_{1-4} alkoxy, R^3 represents nitro, R^4 , R^5 , and R^6 represent a hydrogen atom, and A represents group (i) wherein i is an integer of 1 to 3 and R^{13} and R^{14} , which may be the same or different, represent C_{1-4} alkyl, or may form a five- to seven-membered saturated heterocyclic ring optionally substituted by C_{1-4} alkyl together with the nitrogen atom to which they are attached.
9. The compound according to claim 1, wherein X represents N, Z represents CH, R^1 and R^2 represent C_{1-4} alkoxy, R^3 represents nitro, R^4 , R^5 , and R^6 represent a hydrogen atom, and A represents group (i) wherein i is an integer of 1 to 3 and R^{13} and R^{14} , which may be the same or different, represent C_{1-4} alkyl, or may form a five- to seven-membered saturated heterocyclic ring optionally substituted by C_{1-4} alkyl together with the nitrogen atom to which they are attached.
10. The compound according to claim 1, wherein X represents N, Z represents CH, R^1 and R^2 represent C_{1-4} alkoxy, R^3 represents nitro, R^4 , R^5 , and R^6 represent a hydrogen atom, and A represents group (i) wherein i is 2 and R^{13} and R^{14} , which may be the same or different, represent C_{2-3} alkyl, or may form a six-membered saturated heterocyclic ring optionally substituted by C_{1-4} alkyl together with the nitrogen atom to which they are attached.
11. The compound according to claim 1, wherein R^1 and R^2 represent C_{1-4} alkoxy and A represents group (ii) wherein j is 1 or 2, k is 1 or 2, m is 1 or 2, and R^{15} represents optionally substituted phenyl.
12. The compound according to claim 1, wherein R^1 and R^2 represent C_{1-4} alkoxy, R^3 , R^4 , R^5 , and R^6 represent a hydrogen atom, and A represents group (ii) wherein j is 1 or 2, k is 1 or 2, m is 1 or 2, and R^{15} represents optionally substituted phenyl.
13. The compound according to claim 1, wherein R^1 and R^2 represent C_{1-4} alkoxy, R^3 represents a group other than a hydrogen atom, R^4 , R^5 , and R^6 represent a hydrogen atom, and A represents group (ii) wherein j is 1 or 2, k is 1 or 2, m is 1 or 2, and R^{15} represents optionally substituted phenyl.

14. The compound according to claim 1, wherein R¹ and R² represent C₁₋₄ alkoxy and A represents group (iii) wherein n is 0 (zero); p is an integer of 1 to 3; and R¹⁶ and R¹⁷, which may be the same or different, represent C₁₋₄ alkyl, or may form a five- to seven-membered saturated heterocyclic ring optionally substituted by C₁₋₄ alkyl or an oxygen atom together with the nitrogen atom to which they are attached.
15. The compound according to claim 1, wherein R¹ and R² represent C₁₋₄ alkoxy, R³, R⁴, R⁵ and R⁶ represent a hydrogen atom, and A represents group (iii) wherein n is 0 (zero); p is an integer of 1 to 3; and R¹⁶ and R¹⁷, which may be the same or different, represent C₁₋₄ alkyl, or may form a five- to seven-membered saturated heterocyclic ring optionally substituted by C₁₋₄ alkyl or an oxygen atom together with the nitrogen atom to which they are attached.
16. The compound according to claim 1, wherein R¹ and R² represent C₁₋₄ alkoxy, R³ represents a group other than a hydrogen atom, R⁴, R⁵ and R⁶ represent a hydrogen atom, and A represents group (iii) wherein n is 0 (zero), p is an integer of 1 to 3, and R¹⁶ and R¹⁷, which may be the same or different, represent C₁₋₄ alkyl, or may form a five- to seven-membered saturated heterocyclic ring optionally substituted by C₁₋₄ alkyl or an oxygen atom together with the nitrogen atom to which they are attached.
17. The compound according to claim 1, wherein R¹ and R² represent C₁₋₄ alkoxy and A represents group (iv) wherein q is 0 (zero), r is 1 or 2, s is 1 or 2, t is 1 or 2, and R¹⁸ represents optionally substituted phenyl.
18. The compound according to claim 1, wherein R¹ and R² represent C₁₋₄ alkoxy, R³, R⁴, R⁵ and R⁶ represent a hydrogen atom, and A represents group (iv) wherein q is 0 (zero), r is 1 or 2, s is 1 or 2, t is 1 or 2, and R¹⁸ represents optionally substituted phenyl.
19. The compound according to claim 1, wherein R¹ and R² represent C₁₋₄ alkoxy, R³ represents a group other than a hydrogen atom, R⁴, R⁵, and R⁶ represent a hydrogen atom, and A represents group (iv) wherein q is 0 (zero), r is 1 or 2, s is 1 or 2, t is 1 or 2, and R¹⁸ represents optionally substituted phenyl.
20. The compound according to claim 1, wherein R¹ and R² represent C₁₋₄ alkoxy and A represents group (v) wherein u is 1 and R¹⁹ represents optionally substituted phenyl, or C₁₋₄ alkyl substituted by optionally substituted phenyl.
21. The compound according to claim 1, wherein R¹ and R² represent C₁₋₄ alkoxy, R³, R⁴, R⁵, and R⁶ represent a hydrogen atom, and A represents group (v) wherein u is 1 and R¹⁹ represents optionally substituted phenyl, or C₁₋₄ alkyl substituted by optionally substituted phenyl.
22. The compound according to claim 1, wherein R¹ and R² represent C₁₋₄ alkoxy, R⁵ represents a group other than a hydrogen atom, R³, R⁴, and R⁶ represent a hydrogen atom, and A represents group (v) wherein u is 1 and R¹⁹ represents optionally substituted phenyl, or C₁₋₄ alkyl substituted by optionally substituted phenyl.
23. The compound according to claim 1, wherein R¹ and R² represent C₁₋₄ alkoxy and A represents group (vi) wherein R²⁰ represents optionally substituted phenyl, or C₁₋₆ alkyl optionally substituted by optionally substituted phenyl.
24. The compound according to claim 1, wherein R¹ and R² represent C₁₋₄ alkoxy and A represents group (vii) wherein R²¹ represents optionally substituted phenyl, or C₁₋₆ alkyl optionally substituted by optionally substituted phenyl.
25. The compound according to claim 1, wherein R¹ and R² represent C₁₋₄ alkoxy and A represents group (viii) wherein w is an integer of 1 to 3, L represents -O-, M represents -O- or -C(=O)-O-, and R²² represents optionally substituted phenyl.
26. The compound according to claim 1, wherein R¹ and R² represent C₁₋₄ alkoxy and A represents group (viii) wherein, when L represents -O-, M represents -O-, -C(=O)-O-, -N(-R¹²)-, -C(=O)-N(-R¹²)-, or -C(=O)-; when L represents -S(=O)y- M represents -O-; and, when L represents -N(-R¹¹)-, M represents -O-.
27. The compound according to claim 1, wherein R¹ and R² represent C₁₋₄ alkoxy and A represents group (iii) wherein n is 1 and p is 0 (zero).
28. The compound according to claim 1, wherein R¹ and R² represent C₁₋₄ alkoxy, R³ represents morpholyl, R⁴, R⁵, and R⁶ represent a hydrogen atom, and A represents group (x).

29. A compound selected from the group consisting of the following compounds or pharmacologically acceptable salts or solvates thereof:

N-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}-N'-(2-piperidinoethyl)urea; and
N-[2-(diethylamino)ethyl]-N'-{4-[(6,7-dimethoxy-4-quinazolinyl)oxy]-2-nitrophenyl}urea.

30. A pharmaceutical composition comprising the compound according to any one of claims 1 to 29 or a pharmacologically acceptable salt or solvate thereof.

31. The pharmaceutical composition according to claim 30, for use in the treatment of diseases mediated by the autophosphorylation of a PDGF receptor.

32. The pharmaceutical composition according to claim 31, wherein the disease mediated by the autophosphorylation of the PDGF receptor is selected from the group consisting of ischemic diseases involving blood vessel occlusion or angiostenosis induced by angiopathy; ischemic diseases involving blood vessel occlusion or angiostenosis induced by vascular autotransplantation or allotransplantation; and diseases involving cell proliferation and organ fibrosis induced by PDGF, including chronic rheumatism, PDGF-dependent tumors such as glioma, cirrhosis, pulmonary fibrosis, and occlusion of arteriovenous shunt induced, for example, by dialysis of patients suffering from renal failure.

33. The pharmaceutical composition according to claim 30, for use in the inhibition of angiostenosis.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP00/09157

A. CLASSIFICATION OF SUBJECT MATTER		
Int.Cl. ⁷ C07D215/233, 239/88, 401/12, 403/12, 405/12, A61K31/47, 31/496, 31/5377, 31/505, 31/4709, 31/517, A61P43/00, 9/10		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols)		
Int.Cl. ⁷ C07D215/233, 239/88, 401/12, 403/12, 405/12, A61K31/47, 31/496, 31/5377, 31/505, 31/4709, 31/517, A61P43/00, 9/10		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)		
REGISTRY (STN), CA (STN), CAOLD (STN), CAPLUS (STN)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	EP, 860433, A1 (KIRIN BEER KABUSHIKI KAISHA), 26 August, 1998 (26.08.98) & WO, 97/17329, A1 & US, 6143764, A & AU, 9673400, A	1-4, 30-33 5-29
X Y	US, 5480883, A (Rhone-Poulenc Rorer Pharmaceuticals Inc.), 02 January, 1996 (02.01.96) & WO, 95/15758, A1 & US, 5710158, A & EP, 871448, A1 & AU, 9513050, A	1-3, 30-33 5-29
X Y	KUBO, Kazuo et al., "A novel series of 4-phenoxyquinolines: potent and highly selective inhibitors of PDGF receptor autophosphorylation", Bioorg. Med. Chem. Lett. (1997), Vol.7, No.23, pp.2935-2940	1-4, 30-33 5-29
X	WRIGHT, George C. et al., "Synthesis and hypotensive properties of new 4-aminoquinolines", J. Med. Chem. (1971), Vol.14, No.11, pp.1060-6	1, 2, 30
X	ALSAIDI, Hattab et al., "Convenient synthesis of heteroaryl phenyl ethers from chloropyridines and	1, 2
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 21 March, 2001 (21.03.01)		Date of mailing of the international search report 03 April, 2001 (03.04.01)
Name and mailing address of the ISA/ Japanese Patent Office		Authorized officer
Facsimile No.		Telephone No.

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP00/09157

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	chloroquinolines using phase-transfer catalysis", Synthesis (1980), No.11, pp.921-4	
X	Chemical Abstracts, Vol.58, 4563e	1,2
PX	WO, 00/43366, A (Kirin Brewery Company, Limited.), 27 July, 2000 (27.07.00) (Family: none)	1-33

Form PCT/ISA/210 (continuation of second sheet) (July 1992)